

Form PTO 1390 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (REV 5-93)		ATTORNEY'S DOCKET NUMBER P32331
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED / ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) 10/019105
INTERNATIONAL APPLICATION NO. PCT/EP00/05881	INTERNATIONAL FILING DATE 23 June 2000	PRIORITY DATE CLAIMED 24 June 1999
TITLE OF INVENTION AZOLYLBENZAMIDES AND ANALOGUES AND THEIR USE FOR TREATING OSTEOPOROSIS		
APPLICANT(S) FOR DO/EO/US Carlo FARINA, Stefania GAGLIARDI and Shahzad Sharooq RAHMAN		

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☒ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98; Form PTO-1449, and a copy of the International Search Report.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment.
14. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
15. ☒ Please amend the specification by inserting before the first line the sentence: This is a 371 of International Application PCT/EP00/05881, filed June 23, 2000, which claims priority from the following Great Britain Application: GB 9914825.6, filed June 24, 1999.
16. ☐ A substitute specification.
17. ☐ A change of power of attorney and/or address letter.
18. ☒ An Abstract on a separate sheet of paper.
19. ☐ Other items or information:

PCT/EP00/05881

20 DEC 2001

US APPLICATION NO. 107019105 (for known see 37 CFR 1.50)		INTERNATIONAL APPLICATION NO. PCT/EP00/05881		ATTORNEYS DOCKET NO. P32331	
20. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS PTO USE ONLY	
Basic National Fee (37 C.F.R. 1.492(a)(1)-(5)):				\$890.00	
Search Report has been prepared by the EPO or JPO \$890.00					
International Preliminary Examination Fee paid to USPTO (37 CFR 1.492) \$710.00					
No International Preliminary Examination Fee paid to USPTO (37 CFR 1.492) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) \$740.00					
Neither International Preliminary Examination Fee (37 CFR 1.492) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$1,040.00					
International Preliminary Examination Fee paid to USPTO (37 CFR 1.492) and all claims satisfied provisions of PCT Article 33(2)-(4) \$100.00					
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$890.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$0.00	
Claims	Number Filed	Number Extra	Rate		
Total claims	12 - 20 =	0	0 x \$18.00	\$0.00	
Independent claims	1 - 3 =	0	0 x \$84.00	\$0.00	
Multiple dependent claims (if applicable)			+ \$280.00	\$0.00	
TOTAL OF ABOVE CALCULATIONS =				\$890.00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				\$	
SUBTOTAL =				\$890.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)) +				\$	
TOTAL NATIONAL FEE =				\$890.00	
				Amount to be refunded	\$
				charged	\$

- a. ☐ A check in the amount of \$_____ to cover the above fees is enclosed.
- b. ☒ Please charge my Deposit Account No. 19-2570 in the amount of **\$890.00** to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 19-2570. A duplicate copy of this sheet is enclosed.
- d. ☒ General Authorization to charge any and all fees under 37 CFR 1.16 or 1.17, including petitions for extension of time relating to this application (37 CFR 1.136 (a)(3)).

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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10/019105
531 Rec'd PCT 20 DEC 2001

"EXPRESS MAIL CERTIFICATE"
"EXPRESS MAIL" MAILING LABEL NUMBER EM165003975US
DATE OF DEPOSIT December 20, 2001

Attorney Docket No.: P32331

IN THE UNITED STATES DESIGNATED OFFICE

December 20, 2001

International Application No.: PCT/EP00/05881
International Filing Date: 23 June 2000
Priority Date Claimed: 24 June 1999
Applicant for DO/US: GlaxoSmithKline S.p.A. (formerly SmithKline
Beecham S.p.A.) and SmithKline Beecham p.l.c.
Title of Invention: AZOLYLBENZAMIDES AND ANALOGUES AND
THEIR USE FOR TREATING OSTEOPOROSIS

Commissioner of Patents and Trademarks
Box PCT (DO/US)
Washington D.C. 20231

PRELIMINARY AMENDMENT

Preliminary to the examination of this application, applicants respectfully request amendment of the above-identified application as follows:

In the Claims

Kindly cancel claims 9-15, without prejudice or disclaimer.

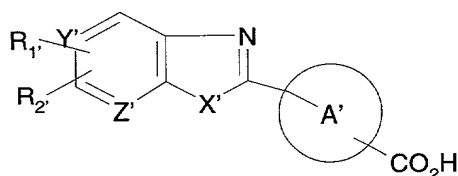
Please amend claims 2-6 and 8 to read as follows:

2. (Amended) A process for the preparation of a compound of formula (I) according to claim 1, or a salt thereof or a solvate thereof, wherein said process comprises the steps of:

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(a) amidation of a carboxylic acid having the formula:



wherein X', Y', Z', A', R1' and R2' each respectively represent X, Y, Z, A, R1 and R2 as defined in claim 1 or a protected form thereof,

with an amine having the formula:



wherein RS' and RT' each respectively represent RS and RT as defined in claim 1, or a protected form thereof, and

(b) optionally preparing a salt or a solvate thereof.

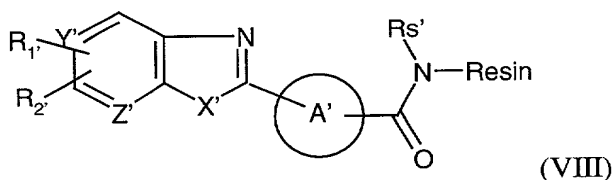
3. (Amended) A process for the preparation of a compound of formula (I) according to claim 2, further comprising the steps of:

- (i) converting the compound of formula (I) formed in step(a) or step (b) into another compound of formula (I);
- (ii) removing any protecting group; and
- (iii) preparing a salt or a solvate thereof.

4. (Amended) A process for the preparation of a compound of formula (I) according to claim 1, or a salt thereof or a solvate thereof, wherein said process comprises cleavage of a compound of formula (VIII) at the N-Resin bond

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wherein X' , Y' , Z' , A' , R_1' and R_2' , and $R_{S'}$ each respectively represent X , Y , Z , A , R_1 , R_2 and R_S as defined in claim 1.

5. (Amended) A pharmaceutical composition comprising a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, and a pharmaceutically acceptable carrier therefor.

6. (Amended) A method for the treatment or prophylaxis of diseases associated with over activity of osteoclasts in mammals wherein said method comprises the administration of an effective non-toxic amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof.

8. (Amended) A method for the treatment of tumours, viral conditions, ulcers, autoimmune diseases and transplantation, for the treatment or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS, Alzheimer's disease, and angiogenic diseases in a human or non-human mammal, which method comprises administering an effective, non-toxic, amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, to a human or non-human mammal in need thereof.

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Please add new claims 16-19, as follows:

16. (New) The method according to claim 8, wherein the treatment of tumours comprises treatment of renal cancer, melanoma, colon cancer, lung cancer and leukemia.

17. (New) The method according to claim 8, wherein the treatment of viral conditions comprises treatment of Semliki Forest virus, Vesicular Stomatitis, Newcastle Disease, Influenza A and B and HIV viruses.

18. (New) The method according to claim 8, wherein the treatment of ulcers comprises treatment of chronic gastritis and peptic ulcers induced by Helicobacter pylori.

19. (New) The method according to claim 8, wherein the treatment of angiogenic diseases comprises treatment of rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours.

REMARKS

The above-identified application is being entered into the National Phase from PCT application no. PCT/EP00/05881.

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Applicants have amended claims 2-6 and 8 and have cancelled claims 9-15 and have added claims 16-19 to put the claims in conformity with U.S. practice. Support for claims 16-19 may be found in original claim 8. No new matter has been introduced.

Respectfully submitted,

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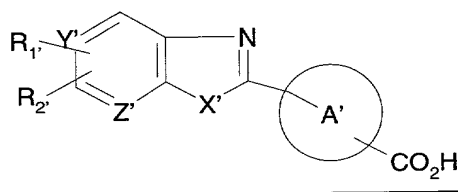
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

2. (Amended) A process for the preparation of a compound of formula (I) [as defined in] according to claim 1, or a salt thereof or a solvate thereof, [which] wherein said process comprises the steps of:

(a) [the] amidation of a [suitable] carboxylic acid having the formula:



wherein X', Y', Z', A', R1' and R2' each respectively represent X, Y, Z, A, R1 and R2 as defined in claim 1 or a protected form thereof,

with [a suitable] an amine having the formula:

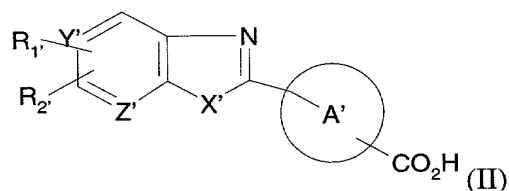


wherein Rs' and Rt' each respectively represent Rs and Rt as defined in claim 1, or a protected form thereof, and

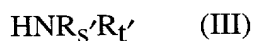
(b) optionally preparing a salt or a solvate thereof.

3. (Amended) A process for the preparation of a compound of formula (I) [as defined in claim 1, or a salt thereof or a solvate thereof, which process comprises the amidation of a compound of formula (II)

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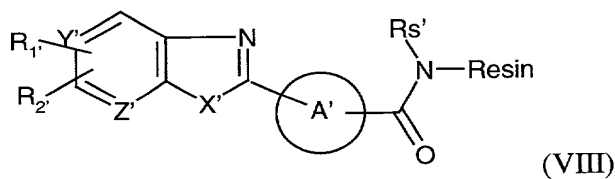
wherein X', Y', Z', A', R₁' and R₂' each respectively represent X, Y, Z, A, R₁ and R₂ respectively as defined in relation to formula (I) as defined in claim 1 or a protected form thereof with a compound of formula (III)



wherein R_S' and R_T' represent R_S and R_T respectively as defined in relation to formula (I) as defined in claim 1 or a protected form thereof and thereafter, as necessary, carrying out one or more of the following steps;] according to claim 2, further comprising the steps of:

- (i) converting [one] the compound of formula (I) formed in step(a) or step (b) into another compound of formula (I);
- (ii) removing any protecting group; and
- (iii) preparing a salt or a solvate [of the compound so formed] thereof.

4. (Amended) A process for the preparation of a compound of formula (I) [as defined in] according to claim 1, or a salt thereof or a solvate thereof, [which] wherein said process comprises [the] cleavage of a compound of formula (VIII) at the N-Resin bond[.]



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wherein X', Y', Z', A', R₁', R₂', and [Rs'] each respectively represent X, Y, Z, A, R₁, R₂ and R_s [Rs respectively as defined in relation to formula (I)] as defined in claim 1.

5. (Amended) A pharmaceutical composition comprising a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof[, or a pharmaceutically acceptable solvate thereof, and a pharmaceutically acceptable carrier therefor.

6. (Amended) A method for the treatment [and/or] or prophylaxis of diseases associated with over activity of osteoclasts in mammals [which] wherein said method comprises the administration of an effective non-toxic amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof.

8. (Amended) A method for the treatment of tumours, [especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia,] viral conditions [(for example those involving Semliki Forest, Vesicular Stomatitis, Newcastle Disease, Influenza A and B, HIV viruses)], ulcers [(for example chronic gastritis and peptic ulcer induced by Helicobacter pylori)], autoimmune diseases and transplantation, for the treatment [and/or] or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS [and], Alzheimer's disease, and angiogenic diseases[, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours,] in a human or non-human mammal, which method comprises administering an effective, non-toxic, amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a

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pharmaceutically acceptable solvate thereof, to a human or non-human mammal in need thereof.

Please add new claims 16-19, as follows:

16. (New) The method according to claim 8, wherein the treatment of tumours comprises treatment of renal cancer, melanoma, colon cancer, lung cancer and leukemia.

17. (New) The method according to claim 8, wherein the treatment of viral conditions comprises treatment of Semliki Forest virus, Vesicular Stomatitis, Newcastle Disease, Influenza A and B and HIV viruses.

18. (New) The method according to claim 8, wherein the treatment of ulcers comprises treatment of chronic gastritis and peptic ulcers induced by *Helicobacter pylori*.

19. (New) The method according to claim 8, wherein the treatment of angiogenic diseases comprises treatment of rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours.

40019465-1-EP001

AZOLYLBENZAMIDES AND ANALOGUES AND THEIR USE
FOR TREATING OSTEOPOROSIS

This invention relates to certain novel compounds, to a process for preparing such compounds, to pharmaceutical compositions containing such compounds and to the use of such compounds and compositions in medicine.

Diseases associated with loss of bone mass are known to be caused by over activity of osteoclast cells. It is also known that certain compounds, usually related to bafilomycin, are useful for treating such diseases. For example International Application Publication Number WO 91/06296 (Astra Aktiebolaget) discloses certain bafilomycin macrolides for the treatment of bone affecting diseases.

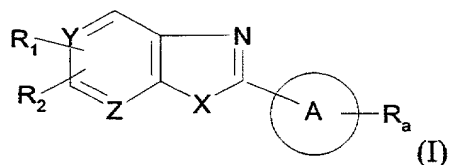
However, bafilomycin derivatives are not selective for osteoclasts in humans. The use of these compounds is therefore associated with unacceptable toxicity due to generalised blockade of other essential v-ATPases. Indeed, to date there is no known treatment which is selective for the human osteoclasts.

The search for a successful treatment for diseases associated with loss of bone mass in humans is further complicated in that the nature of the therapeutic target for the selective inhibition of the osteoclasts is controversial. Thus Baron *et al.* (International Application Publication Number WO 93/01280) indicate that a specific vacuolar ATPase (v-ATPase) has been identified in osteoclasts as a potential therapeutic target. However, the Baron work was carried out in chickens and Hall *et al.* (*Bone and Mineral* 27, 159-166, (1994)), in a study relating to mammals, conclude that in contrast to avian osteoclast v-ATPase, mammalian osteoclast v-ATPase is pharmacologically similar to the v-ATPase in other cells and, therefore, it is unlikely to be a good therapeutic target.

WO 95/30659 (Warner-Lambert Company) discloses certain benzimidazole and imidazopyridine derivatives as dopaminergic agents.

We have now found a group of compounds which are selective for mammalian osteoclasts, acting to selectively inhibit their bone resorbing activity. These compounds are therefore considered to be particularly useful for the treatment and/or prophylaxis of diseases associated with loss of bone mass, such as osteoporosis and related osteopenic diseases, Paget's disease, hyperparathyroidism and related diseases. These compounds are also considered to possess anti-tumour activity, antiviral activity (for example against *Semliki Forest*, *Vesicular Stomatitis*, *Newcastle Disease*, *Influenza A and B*, *HIV* viruses), antiulcer activity (for example the compounds may be useful for the treatment of chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), immunosuppressant activity, antilipidemic activity, antiatherosclerotic activity and to be useful for the treatment of AIDS and Alzheimer's disease. Furthermore, these compounds are also considered useful in inhibiting angiogenesis i.e. the formation of new blood vessels which is observed in various types of pathological conditions (*angiogenic diseases*) such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours.

Accordingly, the invention provides a compound of formula (I)



or a salt thereof, or a solvate thereof, wherein;

X represents oxygen, sulphur, or NR_b wherein R_b represents hydrogen,
 5 unsubstituted or substituted C_{1-6} alkyl, or C_{1-6} alkylcarbonyl wherein the alkyl moiety
 may be unsubstituted or substituted;

Y and Z each independently represent nitrogen, CH, CR_1 or CR_2 ;

A represents an unsubstituted or substituted aryl group or an unsubstituted or
 substituted heterocyclyl group;

10 R_a represents $-\text{C}(\text{O})\text{NR}_s\text{R}_t$ wherein R_s and R_t each independently represent
 hydrogen, unsubstituted or substituted C_{1-6} alkyl, unsubstituted or substituted C_3 -
 gycycloalkyl, unsubstituted or substituted C_{1-6} alkenyl, unsubstituted or substituted aryl,
 aryl C_{1-6} alkyl wherein both the aryl and alkyl moieties may be unsubstituted or
 substituted, unsubstituted or substituted heterocyclyl or an unsubstituted or substituted
 15 heterocyclyl C_{1-6} alkyl group, or R_s and R_t together with the nitrogen to which they are
 attached form a heterocyclyl group;

R_1 and R_2 each independently represents hydrogen, hydroxy, amino, C_{1-6} alkoxy,
 aryloxy wherein the ary moiety may be unsubstituted or substituted, unsubstituted or
 substituted benzyloxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo, trifluoromethyl,
 20 trifluoromethoxy, nitro, C_{1-6} alkyl, carboxy, alkoxycarbonyl, carbamoyl, C_{1-6}
 alkylcarbamoyl, or R_1 and R_2 together represent methylenedioxy, $-(\text{CH}=\text{CH})_{2-3}$ -,
 carbonyldioxy or carbonyldiamino.

Examples of aryl groups represented by A include phenyl.

Examples of heterocyclyl groups represented by A include thiophene.

25 Preferably, A is unsubstituted or substituted phenyl or unsubstituted or substituted
 thiophenyl.

Suitably, R_1 and R_2 each independently represents hydrogen, trifluoromethyl,
 methyl, hydroxy or methoxy or a halogen substituent, for example chloro, bromo or
 fluoro.

30 Suitable positions for substitution for R_1 or R_2 are the 4, 5, 6 or 7 position,
 favourably the 5 or 6 position.

Preferably, R_1 is bromo, chloro, especially 5-chloro, or methyl.

Preferably, R_2 is chloro, especially 6-chloro; or methyl, especially 6-methyl.

Suitably, X represents NR_b .

35 Favourably, X represents NH.

Favourably, Y represents CR_1 .

Favourably, Z represents CH.

When R_s or R_t represent C_{1-6} alkyl favourable groups are ethyl, propyl or butyl.

When R_s or R_t represent substituted C_{1-6} alkyl, favoured groups are 3-aminopropyl, 3-hydroxypropyl, diethylaminoethyl, diethylaminopropyl, morpholinopropyl, 2-(di C_{1-6} alkylamino)ethyl, 3-(di C_{1-6} alkyl)aminopropyl, 4-(di C_{1-6} alkyl)aminobutyl, 3-[4-(3-chlorophenyl)piperazin-1-yl]propyl, 3-[4-(2-methoxy-5-chlorophenyl)piperazin-1-yl]propyl, 3-[4-(2-pyrimidinyl)piperazin-1-yl]propyl, 3-heterocyclylmethyl, (3-pyridyl)methyl, heterocyclylethyl or heterocyclylpropyl groups.

When R_s or R_t represent substituted cycloalkyl, suitable substituents include hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, and halogen.

When R_s or R_t represent heterocyclyl, a favoured group is 3-quinuclidyl or 1-azabicyclo[2.2.2]octan-3-yl.

Suitably, R_s represents 3-pyridyl, 2-methoxy-5-pyridyl, unsubstituted or substituted heterocyclyl and unsubstituted or substituted aryl.

In a favoured aspect, R_s represents an unsubstituted or substituted piperidinyl group, especially a 4-piperidinyl group, or a piperazinyl group, especially a piperazin-1-yl group either unsubstituted or substituted, especially at position 4.

Substituents for the piperidinyl ring of R_s include C_{1-6} alkyl, aryl C_{1-6} alkyl, fused C_{3-8} cycloalkyl, hydroxy C_{1-6} alkyl, and polyhydroxy C_{1-6} alkyl.

Favoured substituents for piperidinyl groups are C_{1-6} alkyl groups, especially methyl groups.

When the piperidinyl group is substituted it is preferred if the substituents are attached to one or both of the carbon atoms alpha to the nitrogen atom.

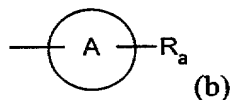
An example of a substituted piperidinyl groups is a 1,2,2,6,6-pentamethylpiperidin-4-yl group, a 2,2,6,6-tetramethylpiperidin-4-yl group, 1-benzylpiperidinyl-4-yl group or a 1-(4-(3-iodobenzoyl)benzyl)piperidin-4-yl group.

Substituents for the piperazinyl group of R_s include unsubstituted or substituted aryl, especially unsubstituted phenyl or phenyl substituted with one or more groups independently selected from halogen, especially chloro; and C_{1-6} alkoxy, especially methoxy.

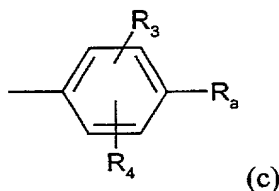
Preferably, R_s is a 1,2,2,6,6-pentamethylpiperidin-4-yl group or a 2,2,6,6-tetramethylpiperidin-4-yl group.

Suitably, R_t is hydrogen.

There is a moiety, referred to herein as moiety (b), which forms part of formula (I) and which has the formula shown below



In one preferred aspect moiety (b) represents a moiety of formula (c)



wherein;

5 R_3 represents hydrogen, hydroxy, C_{1-6} alkoxy, C_{1-6} alkythio, halogen or a group $NR_U R_V$ wherein R_U and R_V each independently represent hydrogen, C_{1-6} alkyl or C_{1-6} alkylcarbonyl.

R_4 represents hydrogen, C_{1-6} alkyl, or C_{1-6} alkoxy.

Suitably R_3 is located meta to R_a .

10 An example of R_3 is hydrogen, methoxy, ethoxy, methyl, chloro, fluoro and bromo.

Favourably, R_3 is methoxy, ethoxy, methyl, *iso*-propoxy, or bromo.

Favourably, R_4 is hydrogen or methoxy.

In a preferred aspect, R_3 and R_4 are not both hydrogen.

15 Alkyl groups referred to herein, including those forming part of other groups, include straight or branched chain alkyl groups containing up to six carbon atoms, said carbon atoms being optionally substituted with up to five, suitably up to three, groups selected from the list consisting of aryl, heterocyclyl, alkylthio, alkoxy, arylalkoxy, amino, mono- or di-alkylamino, cycloalkyl, cycloalkenyl, carboxy and esters thereof, mono- or dialkylaminosulphonyl, aminosulphonyl, cyano, alkylcarbonylamino, 20 arylcarbonylamino, hydroxy, and halogen.

Alkenyl and alkynyl groups referred to herein include straight and branched chain alkenyl groups containing from two to six carbon atoms, said carbon atoms being optionally substituted with up to five, suitably up to three, groups including those substituents described hereinbefore for the alkyl group.

25 Cycloalkyl and cycloalkenyl groups referred to herein include groups having between three and eight ring carbon atoms, which carbon atoms are optionally substituted with up to five, suitably up to three, groups including those substituents described hereinbefore for the alkyl group.

30 When used herein the term "aryl" includes phenyl and naphthyl groups, especially phenyl.

Suitable optional substituents for any aryl group include up to three substituents selected from the list consisting of aryl, arylcarbonyl, alkylthio, halo, alkyl, alkenyl, substituted alkenyl, arylalkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkyloxy, hydroxy, hydroxyalkyl, nitro, amino, cyano, cyanoalkyl, mono- and di-N-alkylamino, acyl, 35 acylamino, N-alkylacylamino, acyloxy, carboxy, carboxyalkyl, carboxyalkenyl, carbamoyl, mono- and di-N-alkylcarbamoyl, alkoxycarbonyl, aryloxy, arylthio, aralkyloxy, aryloxycarbonyl, aminosulphonyl, alkylaminosulphonyl, alkylthio,

alkylsulphonyl, cycloalkyl, heterocyclyl, or a group $-NR_U R_V$ wherein R_U and R_V each independently represent hydrogen, alkyl or alkylcarbonyl.

Suitable aralkyl groups include arylC₁₋₃alkyl groups such as phenylethyl and benzyl groups, especially benzyl.

5 Preferably, substituted aralkyl groups are substituted in the aryl moiety.

When used herein the terms "heterocyclyl" and "heterocyclic" suitably include, unless otherwise defined, aromatic and non-aromatic, single and fused, rings suitably containing up to four heteroatoms in each ring, each of which is selected from oxygen, nitrogen and sulphur, which rings, may be unsubstituted or substituted by, for example,
10 up to three substituents. Each ring suitably has from 4 to 7, preferably 5 or 6, ring atoms. A fused heterocyclic ring system may include carbocyclic rings and need include only one heterocyclic ring.

Suitable optional substituents for any heterocyclyl group includes those mentioned herein with respect to the aryl group.

15 As used herein, the term "halogen" or "halo" includes fluoro, chloro, bromo and iodo, suitably fluoro and chloro, favourably chloro.

When used herein "acyl" includes alkyl carbonyl.

Certain of the carbon atoms of the compounds of formula (I) are chiral carbon atoms and may therefore provide stereoisomers of the compound of formula (I). The
20 invention extends to all stereoisomeric forms of the compounds of formula (I) including enantiomers and mixtures thereof, including racemates. The different stereoisomeric forms may be separated or resolved one from the other by conventional methods or any given isomer may be obtained by conventional stereospecific or asymmetric syntheses.

Suitable salts are pharmaceutically acceptable salts.

25 Suitable pharmaceutically acceptable salts include acid addition salts and salts of carboxy groups.

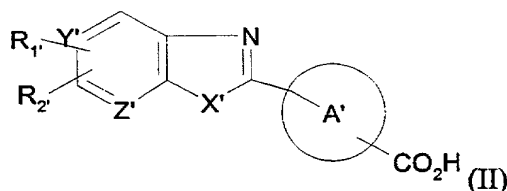
Suitable pharmaceutically acceptable acid addition salts include salts with inorganic acids such, for example, as hydrochloric acid, hydrobromic acid, orthophosphoric acid or sulphuric acid, or with organic acids such, for example as
30 methanesulphonic acid, toluenesulphonic acid, acetic acid, propionic acid, lactic acid, citric acid, fumaric acid, malic acid, succinic acid, salicylic acid, maleic acid, glycerophosphoric acid or acetylsalicylic acid.

Suitable pharmaceutically acceptable salts of carboxy groups include metal salts, such as for example aluminium, alkali metal salts such as sodium or potassium and
35 lithium, alkaline earth metal salts such as calcium or magnesium and ammonium or substituted ammonium salts, for example those with C₁₋₆alkylamines such as triethylamine, hydroxyC₁₋₆alkylamines such as 2-hydroxyethylamine, bis(2-hydroxyethyl)amine or tri(2-hydroxyethyl)amine, cycloalkylamines such as dicyclohexylamine, or with procaine, 1,4-dibenzylpiperidine, N-benzyl-b-
40 phenethylamine, dehydroabietylamine, N,N'-bisdehydroabietylamine, glucamine, N-methylglucamine or bases of the pyridine type such as pyridine, collidine or quinoline.

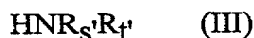
Suitable solvates of the compounds of the formula (I) are pharmaceutically acceptable solvates, such as hydrates.

The salts and/or solvates of the compounds of the formula (I) which are not pharmaceutically acceptable may be useful as intermediates in the preparation of pharmaceutically acceptable salts and/or solvates of compounds of formula (I) or the compounds of the formula (I) themselves, and as such form another aspect of the present invention.

A compound of formula (I) may be prepared by amidation of a suitable carboxylic acid with a suitable amine. Accordingly, the present invention provides a process for the preparation of a compound of formula (I) or a salt thereof or a solvate thereof which process comprises the amidation of a suitable carboxylic acid with a suitable amine. The present invention also provides a process for the preparation of a compound of formula (I) or a salt thereof or a solvate thereof, which process comprises the amidation of a compound of formula (II)



wherein X', Y', Z', A', R₁' and R₂' each respectively represent X, Y, Z, A, R₁ and R₂ respectively as defined in relation to formula (I) or a protected form thereof with a compound of formula (III)



wherein R_S' and R_T' represent R_S and R_T respectively as defined in relation to formula (I) or a protected form thereof and thereafter, as necessary, carrying out one or more of the following steps;

- (i) converting one compound of formula (I) into another compound of formula (I);
- (ii) removing any protecting group;
- (iii) preparing a salt or a solvate of the compound so formed.

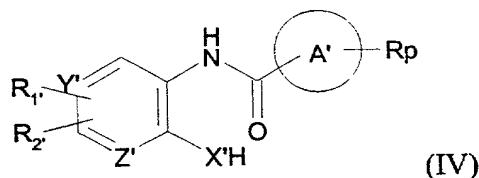
Suitable amidation methods include treating the compound of formula (II) with a compound of formula (III).

The reaction between the compounds of formula (II) and (III) takes place after activation of the carboxyl group.

A carboxyl group may be activated in conventional manner, for example, by conversion into an acid anhydride, acid halide, acid azide or an activated ester such as cyanomethyl ester, thiophenyl ester, p-nitrophenyl ester, p-nitrothiophenyl ester, 2,4,6-trichlorophenyl ester, pentachlorophenyl ester, pentafluorophenyl ester, N-hydroxyphthalimido ester, 8-hydroxypiperidine ester, N-hydroxysuccinimide ester, N-

hydroxybenzotriazole ester, or the carboxyl group may be activated using a carbodiimide such as N,N'-dicyclohexylcarbodiimide (DCC) or 1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride (WSC), either in the presence or the absence of hydroxybenzotriazole (HOBt) or 1-hydroxy-7-azabenzotriazole (HOAt) or it may be activated using N,N'-carbonyldiimidazole, Woodward-K reagent, Castro's reagent or an isoxazolium salt.

A compound of formula (II) may be prepared by cyclising a compound of formula (IV)



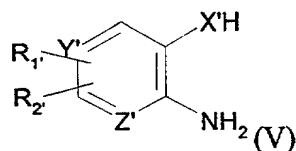
wherein X', Y', Z', A', R₁' and R₂' are as defined in relation to formula (II) and R_p represents a protected carboxyl group or a group convertible into a carboxyl group; and thereafter, as required, converting the group R_p into a carboxyl group.

Suitably, the cyclisation reaction is carried out in an inert hydrocarbon solvent, such as xylene, in presence of a dehydrating agent such as P₂O₅, p-toluensulfonic acid or polyphosphoric acid at any temperature providing a suitable rate of formation of the required product, preferably at an elevated temperature, such as the reflux temperature of the solvent.

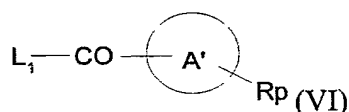
When R_p is a protected carboxyl group, suitable groups include lower alkoxycarbonyl groups, for example methoxy- or ethoxycarbonyl groups, which may be removed by conventional hydrolysis methods, for example by use of basic hydrolysis using ethanolic potassium hydroxide.

When R_p is a group convertible into a carboxyl group, suitable groups include the cyano group. Such groups may be converted into carboxyl groups using conventional methods for example when R_p is a cyano group it may be converted into a carboxyl group by hydrolysis using conventional methods, for example by use of basic hydrolysis using potassium hydroxide solution in ethanol at reflux. A preferred value of R_p is a cyano group.

A compound of formula (IV) is prepared by reacting a compound of formula (V)



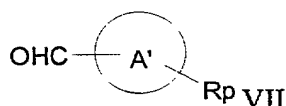
wherein X', Y', Z', R₁' and R₂' are as defined in relation to formula (II) with a compound of formula (VI)



wherein A' and R_p are as defined in relation to formula (IV) and L₁ represents a leaving group, such as a halogen group, for example a chloro group.

The reaction between the compounds of formula (V) and (VI) may be carried in an inert hydrocarbon solvent, such as dichloromethane, at any temperature providing a suitable rate of formation of the required product, preferably at room temperature and in presence of a base, preferably a tertiary amine such as triethylamine.

Alternatively compounds of formula II can be prepared by treating compound of formula V with compounds of formula VII following the procedure described in *Synthetic Communications* 1990, 20, 955-963.



wherein A' and R_p are as defined in relation to formula (IV).

The compounds of formula (V) are known, commercially available, or they are prepared using methods analogous to those used to prepare known compounds, such as those described in *J. March, Advanced Organic Chemistry*, 3rd Edition (1985), Wiley Interscience.

The compounds of formula (VI) are known, commercially available, or they are prepared using methods analogous to those used to prepare known compounds, such as those described in *J. March, Advanced Organic Chemistry*, 3rd Edition (1985), Wiley Interscience.

The compounds of formula (III) are known or they are prepared using methods analogous to those used to prepare known compounds, such as those described in *J. March, Advanced Organic Chemistry*, 3rd Edition (1985), Wiley Interscience.

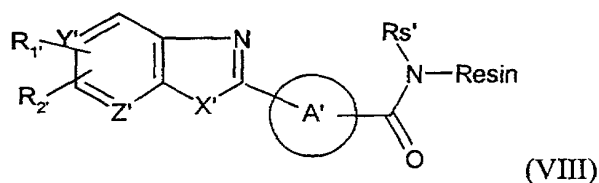
The compounds of formula VII are known or they are prepared using methods described in literature such as those described in *Vogel's Textbook of Practical Organic Chemistry* in the section Aromatic Aldehydes, 5th Edition (1989), Longman Scientific & Technical or in *Chem Ber.*, 1969, 102, 2502-2507; *J. Med. Chem.*, 1997, 40, 2064-2084.

The conversion of one compound of formula (I) with X = NH into another compound of formula (I) with X = NR_p may be carried out using the appropriate conventional procedure; for example the above mentioned conversion may be carried out (i) by reacting the compound of formula (I) with a strong base, for example sodium hydride, in a solvent such as dimethylformamide, followed by alkylation with an alkyl halide or alkyl sulphate or acylation with an acyl halide, or

ii) by reacting the compound of formula (I) with a finely grounded solid base, for example potassium hydroxide, in a solvent such as acetone, followed by alkylation with an alkyl halide or acylation with an acyl halide.

5 Amines of general formula $\text{HNRs}'\text{Rt}'$ may be prepared using the methods known in the art for the preparation of amines, for example as taught in *Houben-Weil, Methoden der Organischen Chemie*, Vol. XI/1 (1957) and Vol. E16d/2 (1992), Georg Thieme Verlag, Stuttgart.

Alternatively a compound of formula (I), wherein X is NR_b , may be prepared by solid phase chemistry after cleavage of a compound of formula (VIII) at the N-Resin bond. Accordingly, in a further aspect, there is provided a process for the preparation of a compound of formula (I), or a salt thereof or a solvate thereof, which process comprises the cleavage of a compound of formula (VIII) at the N-Resin bond.

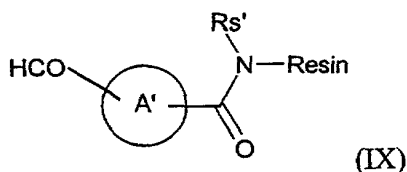


15

wherein X' , Y' , Z' , A' , R_1' , R_2' , and Rs' each respectively represent X, Y, Z, A, R_1 , R_2 and Rs respectively as defined in relation to formula (I).

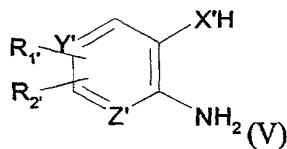
The cleavage reaction is carried out in a suitable mixture of solvents, such as dichloromethane and water, in presence of an organic acid, such as trifluoroacetic acid, at a suitable temperature providing a suitable rate of formation of the required product, preferably at room temperature.

20 A compound of formula (VIII) is prepared by reacting a compound of formula (IX)



25

wherein A' and Rs' are defined in relation of formula (VIII) with a compound of formula (V)

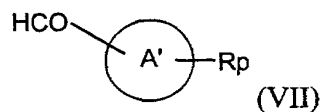


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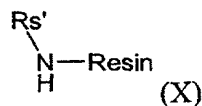
wherein X', Y', Z', R₁' and R₂' are as defined in relation to formula (VIII).

The reaction is carried out in a suitable solvent such as dimethylacetamide (DMA) in presence of a small quantity of organic acid, such as acetic acid, at a suitable temperature providing a suitable rate of formation of the required product, preferably
 5 between 100°C and the reflux temperature of the solvent.

A compound of formula (IX) is prepared by reacting a compound of formula (VII)



- 10 wherein A' and R_p are as defined in relation of formula (IV) with a compound of formula (X)



- 15 wherein Rs' is defined in relation of formula (VIII).

When R_p is a protected carboxyl group, suitable groups include lower alkoxy carbonyl groups, for example methoxy- or ethoxycarbonyl groups, which may be removed by conventional hydrolysis methods, for example by use of basic hydrolysis using ethanolic potassium hydroxide.

- 20 When R_p is a group convertible into a carboxyl group, suitable groups include the cyano group. Such groups may be converted into carboxyl groups using conventional methods for example when R_p is a cyano group it may be converted into a carboxyl group by hydrolysis using conventional methods, for example by use of basic hydrolysis using potassium hydroxide solution in ethanol at reflux.

- 25 The reaction of compound of formula (VII) wherein R_p = -COOH with compound of formula (X) is carried out using suitable amidation methods and takes place after activation of the carboxylic group.

- A carboxyl group may be activated in conventional manner, for example, by conversion into an acid anhydride, acid halide, acid azide or an activated ester such as
 30 cyanomethyl ester, thiophenyl ester, p-nitrophenyl ester, p-nitrothiophenyl ester, 2,4,6-trichlorophenyl ester, pentachlorophenyl ester, pentafluorophenyl ester, N-hydroxyphthalimido ester, 8-hydroxypiperidine ester, N-hydroxysuccinimide ester, N-hydroxybenzotriazole ester, or the carboxyl group may be activated using a carbodiimide such as N,N'-dicyclohexylcarbodiimide (DCC) or 1-ethyl-3-(3-
 35 (dimethylamino)propyl]carbodiimide hydrochloride (WSC), either in the presence or the absence of hydroxybenzotriazole (HOBt) or 1-hydroxy-7-azabenzotriazole (HOAt) or it may be activated using N,N'-carbonyldiimidazole.

A compound of formula (X) is obtained by linking compounds of formula (XI) on suitable resin derived from commercially available Merrifield resin



5

wherein $\text{R}_{\text{S}'}$ represents R_{S} as defined in relation to formula (I).

The resin is prepared by reaction of Merrifield resin with 4-hydroxy-2-methoxybenzaldehyde in a suitable solvent, such as DMF, in presence of a strong base, such as sodium hydride, at any temperature providing a suitable rate of formation of the required product, preferably at a temperature between 50-80°C.

The compounds of formula (XI) are known, commercially available, or they are prepared using methods analogous to those used to prepare known compounds, such as those described in *J. March, Advanced Organic Chemistry*, 3rd Edition (1985), Wiley Interscience.

The reaction between the compounds of formula (III) and the resin prepared as described above is carried out in a suitable solvent, such as DMF, in presence of a catalytic amount of acid, such as acetic acid, in presence of a reducing agent such as sodium triacethoxyborohydride, at a suitable temperature, preferably at room temperature.

A compound of formula (I) or a solvate thereof may be isolated from the above mentioned processes according to standard chemical procedures.

The preparation of salts and/or solvates of the compounds of formula (I) may be performed using the appropriate conventional procedure.

If required mixtures of isomers of the compounds of the invention may be separated into individual stereoisomers and diastereoisomers by conventional means, for example by the use of an optically active acid as a resolving agent. Suitable optically active acids which may be used as resolving agents are described in "*Topics in Stereochemistry*", Vol. 6, Wiley Interscience, 1971, Allinger, N.L. and Eliel, W.L. Eds.

Alternatively, any enantiomer of a compound of the invention may be obtained by stereospecific synthesis using optically pure starting materials of known configuration.

The absolute configuration of compounds may be determined by conventional methods such as X-ray crystallographic techniques.

The protection of any reactive group or atom, may be carried out at any appropriate stage in the aforementioned processes. Suitable protecting groups include those used conventionally in the art for the particular group or atom being protected. Protecting groups may be prepared and removed using the appropriate conventional procedure, for example OH groups, including diols, may be protected as the silylated derivatives by treatment with an appropriate silylating agent such as di-tert-butylsilylbis(trifluoromethanesulfonate): the silyl group may then be removed using conventional procedures such as treatment with hydrogen fluoride, preferably in the form

of a pyridine complex and optionally in the presence of alumina, or by treatment with acetyl chloride in methanol. Alternatively benzyloxy groups may be used to protect phenolic groups, the benzyloxy group may be removed using catalytic hydrogenolysis using such catalysts as palladium (II) chloride or 10% palladium on carbon.

5 Amino groups may be protected using any conventional protecting group, for example tert-butyl esters of carbamic acid may be formed by treating the amino group with di-tert-butyl dicarbonate, the amino group being regenerated by hydrolysing the ester under acidic conditions, using for example hydrogen chloride in aqueous ethanol or trifluoroacetic acid in methylene dichloride. An amino group may be protected as a
10 benzyl derivative, prepared from the appropriate amine and a benzyl halide under basic conditions, the benzyl group being removed by catalytic hydrogenolysis, using for example a palladium on carbon catalyst.

Benzimidazole NH groups and the like may be protected using any conventional group, for example benzenesulphonyl, methylsulphonyl, tosyl, formyl, acetyl (all of them
15 removable by treatment with alkaline reagents), benzyl (removable either with sodium in liquid ammonia or with $AlCl_3$ in toluene), allyl (removable by treatment with rhodium (III) chloride under acidic conditions), benzyloxycarbonyl (removable either by catalytic hydrogenation or by alkaline treatment), trifluoroacetyl (removable by either alkaline or acidic treatment), t-butyl dimethylsilyl (removable by treatment with tetrabutylammonium
20 fluoride), 2-(trimethylsilyl)ethoxymethyl (SEM) (removable by treatment with tetrabutylammonium fluoride in the presence of ethylenediamine), methoxymethyl (MOM) or methoxyethyl (MEM) groups (removed by mild acidic treatment).

Carboxyl groups may be protected as alkyl esters, for example methyl esters, which esters may be prepared and removed using conventional procedures, one
25 convenient method for converting carbomethoxy to carboxyl is to use aqueous lithium hydroxide.

A leaving group is any group that will, under the reaction conditions, cleave from the starting material, thus promoting reaction at a specified site. Suitable examples of such groups unless otherwise specified are halo, mesyloxy, p-nitrobenzenesulphonyloxy
30 and tosyloxy groups.

The salts, esters, amides and solvates of the compounds mentioned herein may as required be produced by methods conventional in the art: for example, acid addition salts may be prepared by treating a compound of formula (I) with the appropriate acid.

Esters of carboxylic acids may be prepared by conventional esterification
35 procedures, for example alkyl esters may be prepared by treating the required carboxylic acid with the appropriate alkanol, generally under acidic conditions.

Amides may be prepared using conventional amidation procedures, for example amides of formula $CONR_{S'}R_{T'}$ may be prepared by treating the relevant carboxylic acid with an amine of formula $HNR_{S'}R_{T'}$ wherein $R_{S'}$ and $R_{T'}$ are as hereinbefore defined.

40 Alternatively, a C_{1-6} alkyl ester such as a methyl ester of the acid may be treated with an amine of the above defined formula $HNR_{S'}R_{T'}$ to provide the required amide, optionally in

presence of trimethylaluminium following the procedure described in *Tetrahedron Lett.* 48, 4171-4173, (1977).

As mentioned above the compounds of the invention are indicated as having useful therapeutic properties.

- 5 Of particular interest is the osteoporosis associated with the peri and post menopausal conditions. Also encompassed are the treatment and prophylaxis of Paget's disease, hypercalcemia associated with bone neoplasms and all the types of osteoporotic diseases as classified below according to their etiology:

10 **Primary osteoporosis**

Involutional

Type I or postmenopausal

Type II or senile

Juvenile

- 15 Idiopathic in young adults

Secondary osteoporosis

Endocrine abnormality

Hyperthyroidism

- 20 Hypogonadism

Ovarian agenesis or Turner's syndrome

Hyperadrenocorticism or Cushing's syndrome

Hyperparathyroidism

Bone marrow abnormalities

- 25 Multiple myeloma and related disorders

Systemic mastocytosis

Disseminated carcinoma

Gaucher's disease

Connective tissue abnormalities

- 30 Osteogenesis imperfecta

Homocystinuria

Ehlers-Danlos syndrome

Marfan's syndrome

Menke's syndrome

- 35 Miscellaneous causes

Immobilisation or weightlessness

Sudeck's atrophy

Chronic obstructive pulmonary disease

Chronic alcoholism

- 40 Chronic heparin administration

Chronic ingestion of anticonvulsant drugs

In addition the invention encompasses the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia, viral conditions (for example those involving *Semliki Forest* virus, *Vesicular Stomatitis* virus, *Newcastle Disease* virus, *Influenza A* and *B* viruses, *HIV* virus), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), for use as immunosuppressant agents in autoimmune diseases and transplantation, antilipidemic agents for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases and to be useful for the treatment of AIDS and Alzheimer's disease. These compounds are also considered useful in treating angiogenic diseases, i.e. those pathological conditions which are dependent on angiogenesis, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours.

Accordingly, present invention provides a method for the treatment and/or prophylaxis of diseases associated with over activity of osteoclasts in mammals which method comprises the administration of an effective non-toxic amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof.

In a further aspect, the present invention provides a method for the treatment or prophylaxis of osteoporosis and related osteopenic diseases in a human or non-human mammal, which method comprises administering an effective, non-toxic, amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, to a human or non-human mammal in need thereof.

In a further aspect, the present invention provides a method for the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia, viral conditions (for example those involving *Semliki Forest*, *Vesicular Stomatitis*, *Newcastle Disease*, *Influenza A* and *B*, *HIV* viruses), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), autoimmune diseases and transplantation, for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS and Alzheimer's disease, angiogenic diseases, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours, in a human or non-human mammal, which method comprises administering an effective, non-toxic, amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, to a human or non-human mammal in need thereof.

In a still further aspect, the present invention a compound of formula (I) or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, for use as an active therapeutic substance.

In further aspect the present invention provides a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for use in the treatment or prophylaxis of diseases associated with over activity of osteoclasts in mammals.

In further aspect the present invention provides a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for use in the treatment or prophylaxis of osteoporosis and related osteopenic diseases.

In a further aspect, the present invention provides a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for use in the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia, viral conditions (for example those involving Semliki Forest, Vesicular Stomatitis, Newcastle Disease, Influenza A and B, HIV viruses), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), autoimmune diseases and transplantation, for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS and Alzheimer's disease, angiogenic diseases, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours, in a human or non-human mammal.

A compound of formula (I), or a pharmaceutically acceptable salt thereof and/or a pharmaceutically acceptable solvate thereof, may be administered per se or, preferably, as a pharmaceutical composition also comprising a pharmaceutically acceptable carrier.

Accordingly, the present invention also provides a pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, and a pharmaceutically acceptable carrier therefor.

Active compounds or a pharmaceutically acceptable salt thereof and/or a pharmaceutically acceptable solvate thereof is normally administered in unit dosage form.

An amount effective to treat the disorders hereinbefore described depends upon such factors as the efficacy of the active compounds, the particular nature of the pharmaceutically acceptable salt or pharmaceutically acceptable solvate chosen, the nature and severity of the disorders being treated and the weight of the mammal. However, a unit dose will normally contain 0.01 to 50 mg, for example 1 to 25 mg, of the compound of the invention. Unit doses will normally be administered once or more than once a day, for example 1, 2, 3, 4, 5 or 6 times a day, more usually 1 to 3 or 2 to 4 times a day such that the total daily dose is normally in the range, for a 70 kg adult of 0.01 to 250 mg, more usually 1 to 100 mg, for example 5 to 70 mg, that is in the range of approximately 0.0001 to 3.5 mg/kg/day, more usually 0.01 to 1.5 mg/kg/day, for example 0.05 to 0.7 mg/kg/day.

In such treatments the active compound may be administered by any suitable route, e.g. by the oral, parenteral or topical routes. For such use, the compound will normally be employed in the form of a pharmaceutical composition in association with a human or veterinary pharmaceutical carrier, diluent and/or excipient, although the exact form of the composition will naturally depend on the mode of administration.

Compositions are prepared by admixture and are suitably adapted for oral, parenteral or topical administration, and as such may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, pastilles, reconstitutable powders,

injectable and infusable solutions or suspensions, suppositories and transdermal devices. Orally administrable compositions are preferred, in particular shaped oral compositions, since they are more convenient for general use.

5 Tablets and capsules for oral administration are usually presented in a unit dose, and contain conventional excipients such as binding agents, fillers, diluents, tableting agents, lubricants, disintegrants, colourants, flavourings, and wetting agents. The tablets may be coated according to well known methods in the art.

10 Suitable fillers for use include cellulose, mannitol, lactose and other similar agents. Suitable disintegrants include starch, polyvinylpyrrolidone and starch derivatives such as sodium starch glycollate. Suitable lubricants include, for example, magnesium stearate. Suitable pharmaceutically acceptable wetting agents include sodium lauryl sulphate.

15 These solid oral compositions may be prepared by conventional methods of blending, filling, tableting or the like. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are, of course, conventional in the art.

20 Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin, hydroxyethylcellulose, carboxymethyl cellulose, aluminium stearate gel or hydrogenated edible fats, emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example, almond oil, fractionated coconut oil, oily esters such as esters of
25 glycerine, propylene glycol, or ethyl alcohol; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid, and if desired conventional flavouring or colouring agents.

30 For parenteral administration, fluid unit dose forms are prepared containing a compound of the present invention and a sterile vehicle. The compound, depending on the vehicle and the concentration, can be either suspended or dissolved. Parenteral solutions are normally prepared by dissolving the compound in a vehicle and filter sterilising before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are also dissolved in the vehicle. To enhance the stability, the composition can be frozen after
35 filling into the vial and the water removed under vacuum.

40 Parenteral suspensions are prepared in substantially the same manner except that the compound is suspended in the vehicle instead of being dissolved and sterilised by exposure to ethylene oxide before suspending in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the active compound.

For topical administration, the composition may be in the form of a transdermal ointment or patch for systemic delivery of the active compound and may be prepared in a

conventional manner, for example, as described in the standard textbooks such as 'Dermatological Formulations' - B.W. Barry (Drugs and the Pharmaceutical Sciences - Dekker) or Harrys Cosmeticology (Leonard Hill Books).

Accordingly, in further aspect, the present invention provides a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for use in the manufacture of a medicament for the treatment or prophylaxis of diseases associated with over activity of osteoclasts in mammals.

In further aspect the present invention also provides a compound of formula (I) or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for use in the manufacture of a medicament for the treatment or prophylaxis of osteoporosis and related osteopenic diseases.

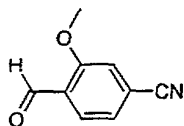
In a further aspect, the present invention also provides the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, for the manufacture of a medicament for the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia., viral conditions (for example those involving Semliki Forest, Vesicular Stomatitis, Newcastle Disease, Influenza A and B, HIV viruses), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), autoimmune diseases and transplantation, for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS and Alzheimer's disease, angiogenic diseases, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours.

No unacceptable toxicological effects are expected with compounds of the invention when administered in accordance with the invention. As is common practice, the compositions will usually be accompanied by written or printed directions for use in the medical treatment concerned.

The following, descriptions, examples and pharmacological methods illustrate the invention but do not limit it in any way.

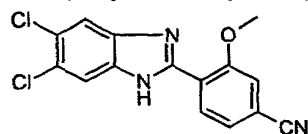
Examples and Descriptions

Preparation 1. 2-Methoxy-4-cyanobenzaldehyde.

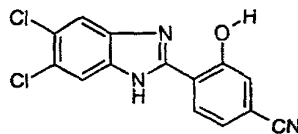


- Thionyl chloride (50 ml) was added to 2-methoxy-4-cyano benzoic acid (*Tetrahedron Letters*, 1986, 27(49), 5997-6000) (8 g, 45.2 mmol) in dichloromethane (70 ml) and the solution was refluxed for 5 h. After cooling to room temperature, the solvent was removed under reduced pressure. The crude benzoyl chloride was dissolved in diglyme (120 ml), cooled at -78°C and 1M lithium tritertbutoxyaluminium hydride in THF (46 ml, 46 mmol) was added dropwise in 3h. Stirring was continued for 30 min at -78°C then the reaction was allowed to reach 0°C and quenched with water (15 ml) and 2N NaOH (15 ml). The reaction mixture was stirred for 1 h, filtered and the organic phase was removed under reduced pressure. The crude residue was purified by column chromatography eluting with n-hexane/ethyl acetate 80:20 to give 4 g of the title compound (yield 55%) as a yellow powder, mp = 112-114°C.
- ¹H-NMR (CDCl₃) δ = 10.5 (s, 1H); 7.93 (d, 1H); 7.30 (d, 1H); 7.16 (s, 1H); 4.01 (s, 3H).

Preparation 2. 5,6-Dichloro-2-(4-cyano-2-methoxyphenyl)benzimidazole (A) and 5,6-dichloro-2-(4-cyano-2-hydroxyphenyl)benzimidazole (B)



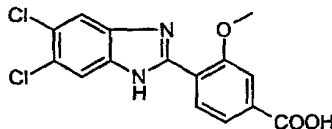
(A)



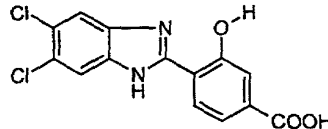
(B)

- A mixture of 2-methoxy-4-cyanobenzaldehyde (3 g, 18.6 mmol), prepared as described in Preparation 1, with 4,5-dichlorophenylendiamine (3.2 g, 18.6 mmol) in nitrobenzene (20 ml) was heated at 160-165°C for 20 h. After cooling to room temperature, n-hexane (300 ml) was added and the mixture was stirred 1 h at room temperature. The mixture was filtered and the solid was washed with additional n-hexane (50 ml). The organic phase was evaporated at reduced pressure to give 3.55 g of a mixture of 5,6-dichloro-2-(4-cyano-2-methoxyphenyl)benzimidazole and 5,6-dichloro-2-(4-cyano-2-hydroxyphenyl)benzimidazole as a brown powder.

- Preparation 3. 5,6-Dichloro-2-(4-carboxy-2-methoxyphenyl)benzimidazole (A) and 5,6-dichloro-2-(4-carboxy-2-hydroxyphenyl)benzimidazole (B).



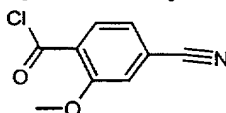
(A)



(B)

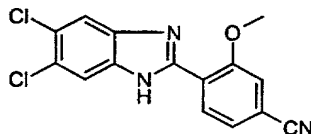
- A mixture of 5,6-dichloro-2-(4-cyano-2-methoxyphenyl)benzimidazole and 5,6-dichloro-2-(4-cyano-2-hydroxyphenyl)benzimidazole (3.5 g), prepared as described in Preparation 2, in ethanol (70 ml) and 2N NaOH (30 ml) was refluxed for 4 h. Solvent was removed under reduced pressure and the residue was treated with 20% HCl (60 ml). The solid was filtered, washed with water (50 ml) and dried at 50°C under vacuum to give 3,2 g of the title compounds.

Preparation 4. 2-Methoxy-4-cyanobenzoyl chloride



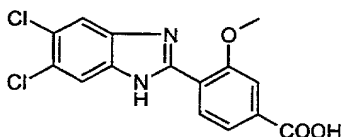
- 2-Methoxy-4-cyanobenzoic acid (*Tetrahedron Letters*, 1986, 27(49), 5997-6000) (1 g, 5.6 mmol) was dissolved in CH₂Cl₂ (20 ml). Oxalyl chloride (1.5 ml, 8.2 mmol) was rapidly introduced into the solution and a drop of DMF was added. A vigorous reaction took place with the abundant evolution of gaseous products. The solution was stirred for 1 h then allowed to stand over night. Solvent was removed using a rotary evaporator to leave 1.1 g of an off white solid (5.6 mmol, yield 99%) that was used without further purification.

Preparation 5. 5,6-Dichloro-2-(4-cyano-2-methoxyphenyl)benzimidazole



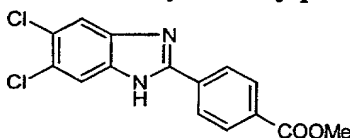
- A solution of 2-methoxy-4-cyanobenzoyl chloride (2 g, 10 mmol) in dichloromethane (20 ml) was added dropwise in 1 h to a solution of 4,5-dichlorophenylendiamine (3.54 g, 20 mmol) and triethylamine (10.1 g = 13.9 ml, 100 mmol) in dichloromethane (20 ml). Stirring was continued for additional two hours. The solvent was removed under vacuum and the residue was triturated with water (50 ml), filtered and dried at 50°C under vacuum. The solid was suspended in diethyl ether (150 ml), stirred for 1 h, filtered and dried under vacuum to give 2.9 g of N-(2-amino-4,5-dichlorophenyl)-2-methoxy-4-cyanobenzamide (yield 43%), mp > 250°C.
- A suspension of N-(2-amino-4,5-dichlorophenyl)-2-methoxy-4-cyanobenzamide (2.9 g, 8.6 mmol) and P₂O₅ (2.9 g, 10 mmol) in xylene (48 ml) was refluxed for 24 h. Additional P₂O₅ (2.9 g, 10 mmol) was added and the mixture was refluxed for 42 h. Solvent was removed under reduced pressure. The residue was treated with 2N NaOH (50 ml) and extracted with ethyl acetate (100 ml). The organic layer was washed with water and brine, dried over Na₂SO₄, filtered and evaporated under reduced pressure to give 2 g of the title compound (yield 73%), mp > 250°C.

Preparation 6. 5,6-Dichloro-2-(4-carboxy-2-methoxyphenyl)benzimidazole



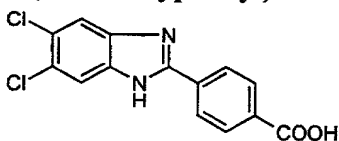
- A solution of 5,6-dichloro-2-(4-cyano-2-methoxyphenyl)benzimidazole, prepared as described in Preparation 5, in ethanol (50 ml) and 2N NaOH (15 ml) was refluxed for 16 h. Solvent was removed under reduced pressure and the residue was acidified with 37% HCl (10 ml), stirred for 1 h. The solid was filtered, washed with water (50 ml), dried at 50°C under vacuum to give 0.92 g of the title compound (yield 46%), mp > 250°C.

Preparation 7. 5,6-Dichloro-2-(4-methoxycarbonylphenyl)benzimidazole



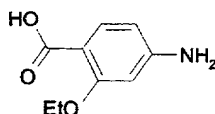
- A mixture of 4,5-dichlorophenyldiamine (4 g, 22.6 mmol) and methyl 4-formylbenzoate (3.68, 22.6 mmol) in nitrobenzene (35 ml) was heated at 140°C for 30 h. After cooling, the mixture was diluted with n-hexane (150 ml) and stirred for 1 h. The solid was filtered obtaining 5 g of the title compound (yield 68.9%) as a brown powder, mp = 240-250°C.

Preparation 8. 5,6-Dichloro-2-(4-carboxyphenyl)benzimidazole

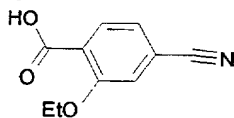


- A mixture of 5,6-dichloro-2-(4-methoxycarbonylphenyl)benzimidazole (2.4 g, 7.47 mmol), prepared as described in Preparation 7, 20% NaOH (7.5 ml, 37.5 mmol) in THF (25 ml) was heated at 50°C for 1 h. After cooling at room temperature, solvent was removed under reduced pressure and pH was adjusted to 5 with acetic acid. The solid that was precipitated was filtered and dried at 50°C to give 2.1 g of the title compound (yield 91.8%) as a brown solid, mp > 250°C.

Preparation 9. 2-Ethoxy-4-aminobenzoic acid

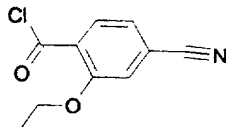


- A suspension of methyl 2-ethoxy-4-acetamidobenzoate (50 g, 211 mmol) in aqueous solution of NaOH (15% W/W, 200 ml) was gently refluxed for 16 hours. The resulting pale brown solution was allowed to cool to room temperature and then further cooled in an ice water bath. Concentrated HCl (37% w/w) was added until the solution reached a pH of 6. The solid precipitated from the solution was filtered under vacuum, dried at 50°C to give 38.3 g of the title compound (yield 100%).

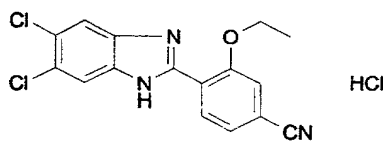
Preparation 10. 2-Ethoxy-4-cyanobenzoic acid

In a 1l reactor equipped with a sealed mechanical stirrer, CuCN (12 g, 134 mmol) were suspended in 100 ml of distilled water. NaCN (18.3 g, 373 mmol) was added with vigorous stirring and the internal temperature was kept below 40°C until all the CuCN went into solution. The suspension of 2-ethoxy-4-aminobenzoic acid (20 g, 110 mmol), prepared as in Preparation 9, in water (200 ml) and concentrated HCl (33 ml) was stirred and cooled in an ice bath. When the temperature reached 5°C, a solution of NaNO₂ (9.7 g, 140 mmol) in water (30 ml) was added dropwise at such a rate as to maintain the temperature below 5 °C.

When all the NaNO₂ was added, the solution was slowly introduced through an ice cooled dropped funnel into the reactor containing the NaCN/CuCN solution. A reaction took place with the vigorous formation of N₂. A few drops of octanol were added to keep the foaming under control. Stirring was continued for 4 h. The resulting suspension was then extracted with ethyl acetate (3x100 ml) and the organic phase dried over MgSO₄ and evaporated under vacuum obtaining 15 g of the title compound (yield 71.1 %) as a light brown powder, mp = 70-172°C.

Preparation 11. 2-Ethoxy-4-cyanobenzoyl chloride

2-Ethoxy-4-cyanobenzoic acid (10 g, 52.3 mmol), prepared as in Preparation 10, and thionyl chloride (50 ml,) were refluxed in CH₂Cl₂ (80 ml) for 5 h. Solvent was removed under vacuum to leave 10.9 g of an off white solid (52 mmol, yield 99%) that was used without further purification.

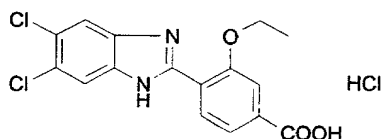
Preparation 12. 5,6-Dichloro-2-(4-cyano-2-ethoxyphenyl)benzimidazole hydrochloride

A solution of 2-ethoxy-4-cyanobenzoyl chloride (10.9 g, 52 mmol), prepared as in Preparation 11, in dichloromethane (109 ml) was added dropwise in 5 h to a solution of 4,5-dichlorophenylendiamine (18.5 g, 104.5 mmol) and triethylamine (53 g = 72.6 ml, 523 mmol) in dichloromethane (550 ml). Stirring was continued for additional 2 h. The solvent was removed under vacuum and the residue was triturated with water (100 ml),

filtered and dried at 50°C under vacuum. The solid was suspended in diethyl ether (200 ml), stirred for 1 h, filtered and dried under vacuum to give 19 g of N-(2-amino-4,5-dichlorophenyl)-2-ethoxy-4-cyanobenzamide (yield 51%), mp = 195-198°C.

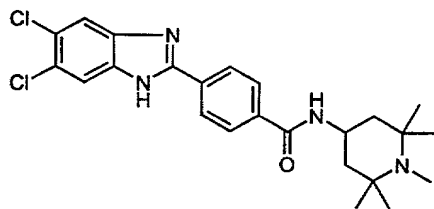
- 5 A suspension of N-(2-amino-4,5-dichlorophenyl)-2-ethoxy-4-cyanobenzamide (19 g, 54.2 mmol) and P₂O₅ (19 g, 134 mmol) in xylene (380 ml) was refluxed for 24 h. Additional P₂O₅ (9.5 g, 67 mmol) was added and the mixture was refluxed for 48 h. Solvent was removed under reduced pressure. The residue was treated with 30% NaOH (80 ml) and water (100 ml) and then acidified with 37% HCl. The solid was filtered, washed with water and dried under vacuum at 50°C to give 16.5 g of the title compound
10 as a light brown powder (yield 82.6%), mp > 250°C.

Preparation 13. 5,6-Dichloro-2-(4-carboxy-2-ethoxyphenyl)benzimidazole hydrochloride



- 15 A mixture of 5,6-dichloro-2-(4-cyano-2-ethoxyphenyl)benzimidazole hydrochloride (16.3 g, 44.2 mmol), prepared as in Preparation 12, 32% NaOH (40 ml) in ethanol (100 ml) was refluxed for 8 h. After cooling to room temperature the organic solvent was removed under vacuum and the aqueous phase was acidified with 37% HCl, stirred for 1 h. The
20 solid was filtered, washed with water (100 ml) and dried at 50°C under vacuum to give 12 g of the title compound as a light brown powder (yield 70%), mp > 250°C.

Example 1. 4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)benzamide



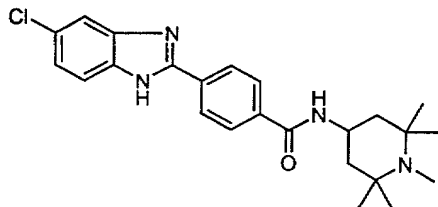
- 25 A mixture of 5,6-dichloro-2-(4-carboxyphenyl)benzimidazole (0.3 g, 0.9 mmol) prepared as described in Preparation 8, 1-hydroxybenzotriazole (0.145 g, 1.08 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (0.207 g, 1.08 mmol) in THF (10 ml) was heated at 35-40°C for 1 h. 1,2,2,6,6-Pentamethyl-4-aminopiperidine in THF
30 (2 ml) was added dropwise and the reaction was refluxed for 1 h. After cooling to room temperature, the solvent was removed under reduced pressure and the residue was treated with 2N NaOH (5 ml). The solid was filtered, washed with water and dried at 50°C under vacuum. The solid was suspended in isopropyl alcohol and stirred for half an hour, filtered and dried to give 91 mg of the title compound (yield 22%) as an yellow powder,
35 mp > 280°C.

¹H-NMR (DMSO-d₆) δ = 13.95 (s br, 1H); 8.30 (d, 1H); 8.23 (d, 2H); 8.00 (d, 2H); 7.89 (s, 2H); 4.30-4.15 (m, 1H); 2.20 (s, 3H); 1.72 (dd, 2H); 1.49 (dd, 2H); 1.10 (s, 6H); 1.07 (s, 6H).

ESI POS; TSQ 700; solvent: methanol / spray 4.5 kV / skimmer: 60 V / capillary 220°C: 459 (MH⁺).

CID Offset = -36 V: 459; 429; 372; 289; 123; 72

Example 2. 4-(5-Chlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-benzamide



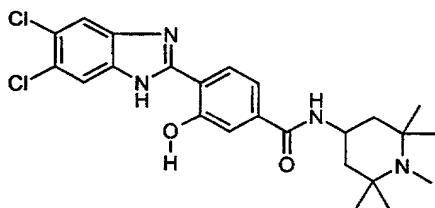
A mixture of 4-(5-chlorobenzimidazol-2-yl)benzoic acid (0.5 g, 1.63 mmol), 1-hydroxybenzotriazole (0.242 g, 1.79 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (0.34 g, 1.89 mmol) in THF (15 ml) was heated for 1 h at 35-40°C. 1,2,2,6,6-Pentamethyl-4-aminopiperidine (0.333g, 1.96 mmol) in THF (3 ml) was added dropwise and the reaction was left 1 h at 60°C. After cooling, the solvent was removed under reduced pressure and the residue was treated with 2N NaOH (15 ml) and extracted with ethyl acetate (20 ml). the organic layer was washed with brine, dried over Na₂SO₄, filtered and evaporated under reduced pressure to give a residue that was treated with CH₃CN. The suspension was stirred for 1 h, filtered and dried at 50°C to give 0.35 g of the title compound (yield 50.5%) as a yellow solid, mp > 250°C.

¹H-NMR (DMSO-d₆) δ = 13.21 (s br, 1H); 8.29 (d, 1H); 8.23 (d, 2H); 8.01 (d, 2H); 7.67 (s br, 1H); 7.62 (d, 1H); 7.25 (dd, 1H); 4.20 (m, 1H); 2.20 (s, 3H); 1.72 (dd, 2H); 1.46 (dd, 2H); 1.10 (s, 2H); 1.06 (s, 6H).

ESI POS; TSQ 700; solvent: methanol / spray 4.5 kV / skimmer: 60 V / capillary 220°C: 425 (MH⁺).

ESI DAU+425-427(Collision gas: Argon): 425; 394; 338; 272; 255; 123; 72.

Example 3. 4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-3-hydroxybenzamide.



A solution of 5,6-dichloro-2-(4-carboxy-2-methoxyphenyl)benzimidazole and 5,6-dichloro-2-(4-carboxy-2-hydroxyphenyl)benzimidazole(0.5 g, 1.48 mmol), prepared as described in Preparation 3, 1-hydroxybenzotriazole (0.21 g, 1.56 mmol) and N-(3-

dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (0.35 g, 1.82 mmol) in THF (20 ml) was refluxed for 5 h. A solution of 1,2,2,6,6-pentamethyl-4-aminopiperidine (0.25 g, 1.5 mmol) in THF (3 ml) was added dropwise and refluxed for 3 h. After cooling to room temperature the solvent was evaporated under vacuum and the crude residue was

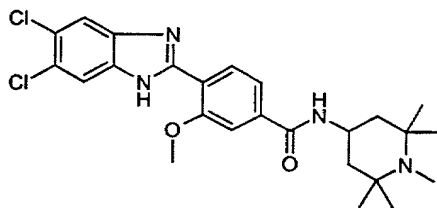
purified by column chromatography eluting with CH₂Cl₂/MeOH/NH₄OH 86:10:0.6 to give 10 mg of the title compound, mp >250°C

¹H-NMR (DMSO-d₆) δ = 12.39 (s br, 1H); 8.10 (d, 1H); 7.92 (d, 1H); 7.89 (s, 2H); 7.50 (s, 1H); 7.48 (d, 1H); 4.30-4.20 (m, 1H); 2.29 (s, 3H); 1.80 (dd, 2H); 1.52 (dd, 2H); 1.14 (s, 6H); 1.11 (s, 6H).

ESI POS; TSQ 700; solvent: methanol/ spray 4.5 kV / skimmer: 60 V/ capillary 220°C: 475 (MH⁺).

CID offset = -42V: 475; 444; 388; 305; 123; 72.

Example 4. 4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-3-methoxybenzamide.



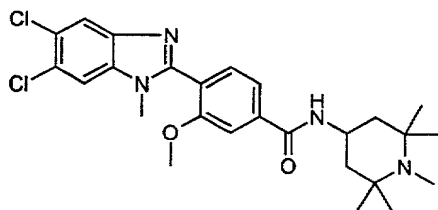
A solution of 5,6-dichloro-2-(4-carboxy-2-methoxyphenyl)benzimidazole (0.8 g, 2.36 mmol), prepared as described in Preparation 6, 1-hydroxybenzotriazole (0.32 g, 2.36 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (0.56 g, 2.9 mmol) in 80 ml of DMF/THF (50:50) was refluxed for 5 h. A solution of 1,2,2,6,6-pentamethyl-4-aminopiperidine (0.5 g, 2.9 mmol) in THF (5 ml) was added dropwise and the reaction was refluxed for additional 3 h. After cooling, solvent was removed under reduced pressure and the residue was treated with 1N NaOH (10 ml) and extracted with dichloromethane (50 ml). The organic layer was washed with water, dried over Na₂SO₄, filtered and evaporated under reduced pressure. The residue was triturated with diisopropyl ether (150 ml), stirred for 1 h, filtered to give 0.55 g of the title compound (yield 47.6%), mp = 285-286°C.

¹H-NMR (DMSO-d₆) δ = 12.40 (s br, 1H); 8.37 (d, 1H); 8.32 (d, 1H); 7.88 (s br, 2H); 7.66 (d, 1H); 7.61 (dd, 1H); 4.22 (m, 1H); 4.10 (s, 3H); 2.19 (s, 3H); 1.73 (dd, 2H); 1.47 (dd, 2H); 1.10 (s, 6H); 1.05 (s, 6H).

ESI POS; TSQ 700; solvent: methanol/ spray 4.5 kV / skimmer: 60 V/ capillary 220°C: 489 (MH⁺).

CID Offset = -45V: 489; 319; 123.

Example 5. 4-(5,6-Dichloro-1-methylbenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-3-methoxybenzamide.



A mixture of 4-(5,6-dichlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-3-methoxybenzamide (0.16 g, 0.33 mmol), prepared as described in Example 4, and KOH (0.0185 g, 0.33 mmol) in acetone (8 ml) was stirred for 1 h at room temperature.

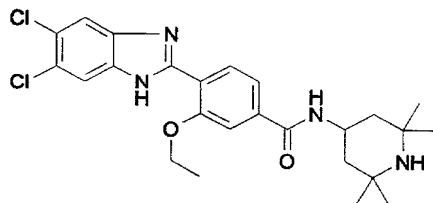
- 5 Iodomethane (0.047 g, 0.033 mmol) was added and stirring was continued for 24 h. Solvent was removed under reduced pressure and the residue was partitioned between water and ethyl acetate. the organic layer was washed with brine, dried over Na₂SO₄, filtered and evaporated under reduced pressure. The crude residue was purified by column chromatography eluting with CH₂Cl₂/MeOH/NH₄OH 95:5:0.2. Fraction
10 containing the desired product were collected, evaporated to dryness under reduced pressure and the solid was triturated with diisopropyl ether to give 0.022 g of the title compound (yield 13%), mp = 178-180°C

¹H-NMR (DMSO-d₆) δ = 8.01 (d br, 1H); 7.91 (s, 1H); 7.89 (s, 1H); 7.64 (d, 1H); 7.61 (dd, 1H); 7.54 (d, 1H); 4.25 (m, 1H); 3.90 (s, 3H); 3.61 (s, 3H); 2.24 (s, 3H); 1.81 (dd, 2H); 1.56 (dd, 1H); 1.15 (s, 6H); 1.09 (s, 6H).

ESI POS; TSQ 700; solvent: methanol / spray 4.5 kV / skimmer: 60 V/ capillary 220°C: 503 (MH⁺); 472; 416.

CID Offset= -67 V: 503; 472; 416; 350; 333; 123; 72.

- 20 **Example 6. 4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide.**



- A mixture of 5,6-dichloro-2-(4-carboxy-2-ethoxyphenyl)benzimidazole hydrochloride (1 g, 2.58 mmol), prepared as in Preparation 11, thionyl chloride (8 ml) in dichloromethane (20 ml) was refluxed for 3 h. After cooling to room temperature the solvent was removed under vacuum and the crude residue was used in following reaction without further purification.

- The acid chloride was added portionwise to a solution of 4-amino-2,2,6,6-tetramethylpiperidine (0.612 g, 3.87 mmol), triethylamine (5 ml, 36 mmol) in dichloromethane (50 ml). Stirring was continued at room temperature for 2 h. The solvent was removed under vacuum and the residue was suspended in water (50 ml) and filtered.
30 The solid was dried at 50°C under vacuum and then crystallised with ethanol to give 0.6 g of the title compound as a light brown powder (yield 47.5%), mp > 280°C.

¹H-NMR (DMSO-d₆) δ = 12.20 (s br, 1H); 8.30 (m, 2H); 7.90 (s, 2H); 7.64 (s, 1H); 7.59 (d, 1H); 4.40 (q, 2H); 4.35-4.22 (m, 1H); 1.73 (d, 2H); 1.50 (t, 3H); 1.20 (dd, 2H); 1.20 (s, 6H); 1.05 (s, 6H).

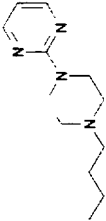
EI; TSQ 700; source 180°C; 70 V; 200 uA: 488 (MH⁺); 473; 124.

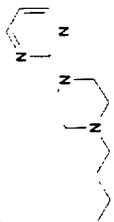
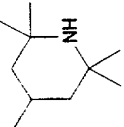
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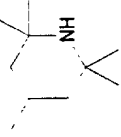
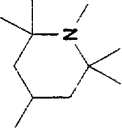
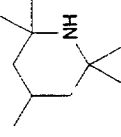
Patent application

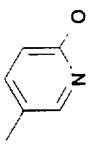
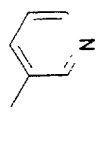
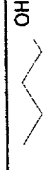
The compounds listed in Table 1 were prepared according to Example 6.

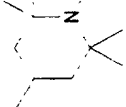
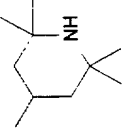
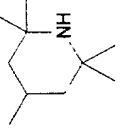
Table 1

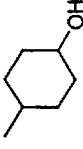
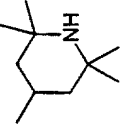
Ex. No	Name	X	Y	Z	R ₁	R ₂	R ₃	R ₄	R ₅	R _i	MP(°C)	N.M.R.	MS
7	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(4-(2-pyrimidinyl)piperazin-1-yl)propyl]-3-methoxybenzamide	NH	CH	CH	5-Cl	6-Cl	OMe	H		H	255-258	¹ H-NMR (DMSO-d ₆) δ = 10.90 (s br, 1H); 8.96 (t, 1H); 8.45 (d, 2H); 8.39 (d, 1H); 7.91 (s, 2H); 7.72 (s, 1H); 7.62 (d, 1H); 6.71 (dd, 1H); 4.71 (d, 2H); 4.12 (s, 3H); 3.60 (d, 2H); 3.50-3.35 (m, 4H); 3.21-3.00 (m, 4H); 2.05 (m, 2H).	A) ESI POS; TSQ 700; solvent: methanol/ spray 4.5 kV / skimmer: 60 V/ capillary 220°C: 540 (MH ⁺). B) CID Offset = -53 V: 540; 376; 319; 122.

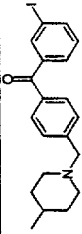
8	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(4-(2-pyrimidinyl)piperazin-1-yl)propyl]-3-hydroxybenzamide	NH	CH	CH	5-Cl	6-Cl	OH	H		H	258-260	¹ H-NMR (DMSO-d ₆) δ = 13.00 (s br, 1H); 8.57 (t, 1H); 8.35 (d, 2H); 8.18 (d, 1H); 7.93 (s br, 2H); 7.52 (s, 1H); 7.49 (d, 1H); 6.61 (dd, 1H); 3.71 (m, 4H); 3.40-3.28 (m, 2H); 2.49-2.39 (m, 6H); 1.80-1.70 (m, 2H).	ESI POS; TSQ 700; solvent: methanol/ spray 4.5 kV / skimmer: 60 V/ capillary 220°C; 526 (M ⁺)
9	4-(5,6-Dichlorobenzimidazol-2-yl)-N,N-dimethyl-3-methoxybenzamide	NH	CH	CH	5-Cl	6-Cl	OMe	H	Me	Me	254-256	¹ H-NMR (DMSO-d ₆) δ = 12.38 (s br, 1H); 8.38 (d, 1H); 7.92 (s br, 1H); 7.80 (s br, 1H); 7.30 (s, 1H); 7.15 (d, 1H); 4.09 (s, 3H); 3.05 (s, 3H); 3.00 (s, 3H).	EI; TSQ 700; 400 mA; 70 V; 363 (M ⁺); 334; 319; 291; 213; 187.
10	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	NH	CH	CH	5-Cl	6-Cl	OMe	H		H	233-235	¹ H-NMR (DMSO-d ₆) δ = 12.40 (s br, 1H); 8.36 (d, 1H); 8.31 (d, 1H); 7.93 (s br, 1H); 7.81 (s br, 1H); 7.66 (d, 1H); 7.61 (dd, 1H); 4.40-4.30 (m, 1H); 4.10 (s, 3H); 1.73 (dd, 2H); 1.21 (dd, 2H); 1.20 (s, 6H); 1.08 (s, 6H).	EI; TSQ 700; 400 mA; 70 V; 474 (M ⁺); 459; 124.

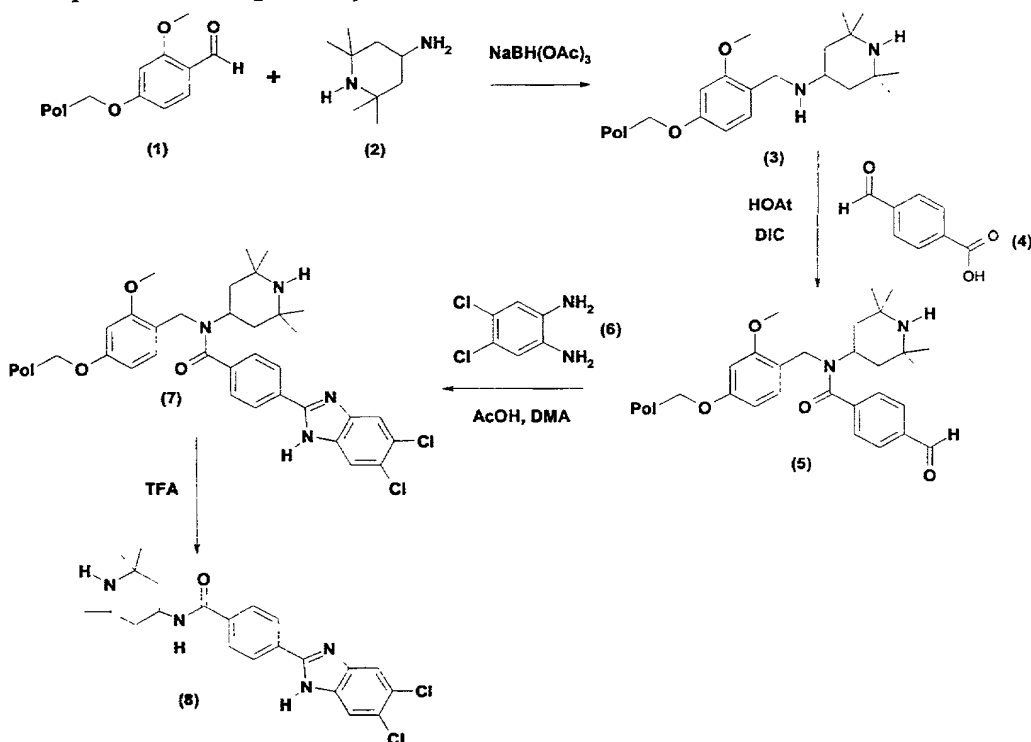
11	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-N-methyl-3-methoxybenzamide	NH	CH	CH	CH	5-Cl	6-Cl	OMe	H		Me	240-242	¹ H-NMR (DMSO-d ₆) δ (343 K) = 12.23 (s br, 1H); 8.34 (d, 1H); 7.84 (s br, 2H); 7.21 (s, 1H); 7.08 (dd, 1H); 4.17-3.91 (m, 1H); 4.06 (s, 3H); 2.84 (s, 3H); 1.54 (dd, 2H); 1.42 (dd, 2H); 1.05 (s, 12H).	EI; TSQ 700; source 180 °C; 70 °V; 200 mA; 473; 124.
12	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-3-ethoxybenzamide	NH	CH	CH	CH	5-Cl	6-Cl	OEt	H		H	>260	¹ H-NMR (DMSO-d ₆) δ: 12.19 (s br, 1H); 8.31 (d br, 1H); 8.28 (d, 1H); 7.93 (s, 1H); 7.85 (s, 1H); 7.64 (s, 1H); 7.59 (d, 1H); 4.41 (q, 2H); 4.30-4.13 (m, 1H); 2.20 (s, 3H); 1.73 (dd, 2H); 1.48 (t, 3H); 1.47 (dd, 2H); 1.11 (s, 6H); 1.06 (s, 6H).	EI; TSQ 700; source 180 °C; 70 °V; 200 mA; 487; 139
13	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	NH	CH	CH	CH	5-Cl	6-Cl	Me	H		H	>250	¹ H-NMR (DMSO-d ₆) δ = 13.05 (s br, 1H); 8.30 (m, 1H); 8.00-7.80 (m, 5H); 4.35-4.25 (m, 1H); 2.68 (s, 3H); 1.79 (d, 2H); 1.24 (s, 12H); 1.12 (m, 2H).	EI; TSQ 700; 400 mA; 70 °V; 458 (M ⁺); 443; 124.

14	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[5-(2-methoxy)pyridyl]-3-ethoxybenzamide	NH	CH	CH	CH	5-Cl	6-Cl	OEt	H		H	219-220	¹ H-NMR (DMSO-d ₆) δ: 12.25 (s, 1H); 10.39 (s, 1H); 8.53 (d, 1H); 8.37 (d, 1H); 8.05 (dd, 1H); 7.96 (s, 1H); 7.87 (s, 1H); 7.76 (s, 1H); 7.73 (d, 1H); 6.87 (d, 1H); 4.47 (q, 2H); 3.86 (s, 3H); 1.50 (t, 3H).	El: TSQ 700; source 180 °C; 70 V; 200 mA: 456 (M ⁺); 441; 333.
15	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-pyridyl)-3-ethoxybenzamide	NH	CH	CH	CH	5-Cl	6-Cl	OEt	H		H	>260	¹ H-NMR (DMSO-d ₆) δ: 12.26 (s, 1H); 10.54 (s, 1H); 8.94 (s, 1H); 8.38 (d, 1H); 8.34 (d, 1H); 8.20 (d, 1H); 7.96 (s, 1H); 7.87 (s, 1H); 7.77 (s, 1H); 7.74 (d, 1H); 7.42 (dd, 1H); 4.47 (q, 2H); 1.50 (t, 3H).	El: TSQ 700; source 180 °C; 70 V; 200 mA: 426 (M ⁺); 411; 333.
16	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-hydroxypropyl)-3-ethoxybenzamide	NH	CH	CH	CH	5-Cl	6-Cl	OEt	H		H	148-150	¹ H-NMR (DMSO-d ₆) δ: 12.19 (s br, 1H); 8.59 (t br, 1H); 8.29 (d, 1H); 7.94 (s, 1H); 7.85 (s, 1H); 7.65 (s, 1H); 7.58 (d, 1H); 4.47 (t, 1H); 4.42 (q, 2H); 3.48 (dt, 2H); 3.35 (dt, 2H); 1.71 (m, 2H); 1.48 (t, 3H).	El: TSQ 700; source 180 °C; 70 V; 200 mA: 407 (M ⁺); 392; 289; 187.

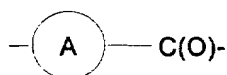
17	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1,2,2,6,6-pentamethylpiperidin-4-yl)-2,5-dimethoxybenzamide	NH	CH	CH	5-Cl	6-Cl	OMe	OMe		H	>250	¹ H-NMR (DMSO-d ₆) δ: 12.38 (s br, 1H); 8.03-7.94 (m, 3H); 7.82 (s, 1H); 7.53 (s, 1H); 4.30-4.10 (m, 1H); 4.02 (s, 3H); 3.94 (s, 3H); 2.20 (s, 3H); 1.76 (dd, 2H); 1.41 (dd, 2H); 1.11 (s, 6H); 1.06 (s, 6H).	El; TSQ 700; source 180 °C; 70 V; 200 mA; 503 ; 349; 138; 124.
18	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2,5-dimethoxybenzamide	NH	CH	CH	5-Cl	6-Cl	OMe	OMe		H	>250	¹ H-NMR (DMSO-d ₆) δ: 12.38 (s br, 1H); 8.03 (d, 1H); 7.99 (s, 1H); 7.97 (s br, 1H); 7.82 (s br, 1H); 7.53 (s, 1H); 4.37-4.21 (m, 1H); 4.03 (s, 3H); 3.94 (s, 3H); 1.78 (s, 3H); 1.76 (dd, 2H); 1.21 (s, 6H); 1.17 (dd, 2H); 1.08 (s, 6H).	El; TSQ 700; source 180 °C; 70 V; 200 mA; 489; 124.
19	4-(5-Chlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	NH	CH	CH	5-Cl	H	OEt	H		H	222-225	¹ H-NMR (DMSO-d ₆) δ: 12.18 and 12.10 (s br, 1H); 8.49 (d br, 1H); 8.30 (d, 1H); 7.72-7.58 (m, 4H); 7.23 (m, 1H); 4.42 (q, 2H); 4.44-4.29 (m, 1H); 1.87 (dd, 2H); 1.48 (t, 3H); 1.48 (dd, 2H); 1.36 (s, 6H); 1.31 (s br, 6H).	ESI POS; AQA; solvent: methanol/ spray 3 kV / skimmer: 20 V/ probe 135 °C: 455 (MH ⁺).

20	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(4-hydroxycyclohex-1-yl)-3-ethoxybenzamide	NH	CH	CH	CH	5-Cl	6-Cl	OEt	H		H	>260	¹ H-NMR (DMSO-d ₆) δ: 12.18 (s, 1H); 8.28 (d br, 1H); 8.27 (d, 1H); 7.94 (s, 1H); 7.85 (s, 1H); 7.62 (d, 1H); 7.58 (dd, 1H); 4.53 (d, 1H); 4.42 (q, 2H); 3.82-3.68 (m, 1H); 3.47-3.35 (m, 1H); 1.92-1.79 (m, 4H); 1.48 (t, 3H); 1.44-1.20 (m, 4H).	A) EI; TSQ 700; source 180 °C; 70 V; 200 mA; 447 (M ⁺); 432; 350; 334; 305; 289. B) ESI POS; AQA; solvent: methanol/ spray 3kV/ skimmer 20V/ probe 135 °C; 448 (MH ⁺).
21	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-isopropoxybenzamide trifluoroacetate	NH	CH	CH	CH	5-Cl	6-Cl	OiPr	H		H	>250	¹ H-NMR (DMSO-d ₆) δ: 11.93 (s br, 1H); 8.30 (d br, 1H); 8.27 (d, 1H); 7.93 (s, 2H); 7.65 (s, 1H); 7.59 (dd, 1H); 4.91 (dt, 1H); 4.38-4.23 (m, 1H); 1.74 (dd, 2H); 1.45 (d, 6H); 1.20 (dd, 2H); 1.20 (s, 6H); 1.08 (s, 6H).	A) EI; TSQ 700; source 180 °C; 70 V; 200 mA; 487; 124.

22	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-(4-(3-iodobenzoyl)benzyl)piperidin-4-yl)-3-ethoxybenzamide	NH	CH	CH	5-Cl	6-Cl	OEt	H		H	122	¹ H-NMR (CDCl ₃) δ: 10.75 (s, br, 1H); 8.6 (d, 1H); 8.15 (s, 1H); 7.95 (m, 2H); 7.75 (m, 3H); 7.68 (m, 2H); 7.5 (d, 2H); 7.35 (d, 1H); 7.25 (d, 1H); 6.11 (d br, 1H); 4.45 (q, 2H); 4.13-4.00 (m, 1H); 3.65 (s, 2H); 2.95 (d, 2H); 2.3 (dd, 2H); 2.1 (d, 2H); 1.76 (m, 2H); 1.65 (t, 3H).
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Example 23. Solid phase synthesis of benzimidazole derivatives**STEP 1 Addition of R_S**

Resin (1) (1.0 g, 1.62 mmol) was suspended in 1% acetic acid in DMF (25 ml) along with 4-Amino-2,2,6,6-tetramethylpiperidine (2) (5 eq, 1.27 g). Sodium triacetoxyborohydride (5 eq, 1.72 g) was then added portionwise and the suspension mixed on a rotator for 20 h. The resulting suspension was then filtered and the resin was washed with DMF (x2), DCM (x2) and methanol (x2) (20 ml each wash). The resulting pale yellow resin (1.2 g) was analysed by MAS NMR (CDCl₃); $\delta = 10.3$ ppm disappears to indicate complete conversion to (3).

**STEP 2 Addition of the moiety**

Resin (3) (500 mg, 0.66 mmol) was suspended in DCM:DMF, 1:1 (10 ml) along with 1-Hydroxy-7-azabenzotriazole (1.1 eq, 99 mg), 4-Carboxybenzaldehyde (4) (1.1 eq, 110 mg) and 1,3-diisopropylcarbodiimide (1.1 eq, 114 μ l). The suspension was mixed on a rotator for 22 h.

The resin was then filtered and washed with DMF (x2), DCM (x2) and methanol (x2) (20 ml each wash). The dried resin was analysed by MAS NMR (CDCl₃); appearance of aldehyde and aromatic signals at $\delta = 10.3$ ppm and $\delta = 8.4-7.6$ ppm indicate conversion to (5).

STEP 3 Formation of fused heterocyclic moiety

Resin (5)(280 mg, 0.31 mmol) was suspended in 5% acetic acid in DMA (6 ml) along with 4,5-Dichloro-1,2-diamine (6). The suspension was then warmed to 120°C with stirring and heated for ~64 h.

- The resin was then filtered and washed with DMA (x2), DMF (x2), DCM (x2), DMA (x3) and methanol (x2)(~15 ml each wash).

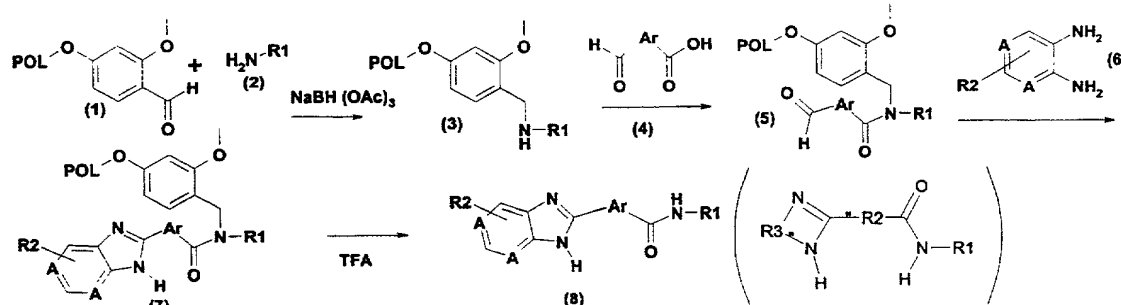
STEP 4 Cleavage

- The resin (7) was suspended in TFA:DCM:water 16:3:1 (7 ml) and mixed for ~1 h. The cleavage solution was then filtered and DCM (2 x 3 ml) used to rinse the resin. The combined filtrates were concentrated to give the benzimidazole (8) (47 mg) in 84% purity by HPLC (UV at 215 nm).

Purification by HPLC gave an orange/white solid which was pure benzimidazole (8)
¹H-NMR (CDCl₃) δ: 7.9-8.8 (aromatic and N-H protons, 9H); 4.4 (methine proton, 1H); 1.6 and 2.0(methylene protons, 4H); 1.44 (methyl protons 12H).

- MS (M+H)⁺ m/z 445.

Preparation 14. Array synthesis



STEP 1 Resin Attachment

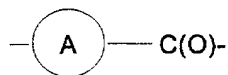
- Merrifield resin (250-300 um, 100 g, 0.2 mol) was suspended in dimethylacetamide (DMA, 1 l) along with 4-Hydroxy-2-methoxybenzaldehyde (2 eq, 60.8 g) and mixed with an overhead stirrer. Sodium hydride (60%, 2 eq, 16.0 g) was slowly added and the resulting brown suspension was heated at 80°C for 18 h.

- After cooling the resin was filtered and washed with DMF (x2), DCM:methanol 1:1 (x2), water (x1), methanol (x1), DCM (x1) and methanol (x3)(500 ml each wash). Drying in a vacuum oven gave the aldehyde (1) as a sand-coloured resin (121 g). Structure confirmed by MAS NMR, δ = 10.3 ppm (aldehyde proton) and δ = 3.8 ppm (methoxy protons).

STEP 2 Addition of R₅

- 12 batches of resin (1)(4 g, 6.48 mmol) were each suspended in 1% acetic acid in DMF (100 ml) along with the relevant amine (2)(5 eq, 32.4 mmol). Sodium triacetoxymethylborohydride (5 eq, 6.9 g) was then added gradually to each flask and the suspensions mixed on an orbital shaker for >19 h.
- The resulting suspensions were filtered and each resin was washed with water (x1), DMF

(x2), DCM (x2) and methanol (x2) (75 ml each wash). The resulting resins were analysed by MAS NMR; $\delta = 10.3$ ppm disappears to indicate complete conversion to (3).



STEP 3 Addition of moiety

- 5 Each of the 12 amine-loaded resins (3) was added to 96 IRORI Microkans equipped with RF-tags (~42 $\mu\text{mol}/\text{kan}$) and these were sorted into 8 batches of 144 kans. Each batch was then suspended in DCM:DMF, 1:1 (120 ml) along with 1-Hydroxy-7-azabenzotriazole (5 eq, 4.0 g), the relevant carboxyaldehyde (4)(5 eq) and 1,3-Diisopropylcarbodiimide (5 eq, 4.7 ml). The suspensions were mixed on an orbital shaker for 22 h.
- 10 The kans were then filtered and washed with DCM (x1), DMF (x2), methanol (x1), DCM (x2), DCM:methanol 1:1 (x1), methanol (x2) and ether (x2)(~500 ml each wash). The dried kans were resorted into 12 batches for the next step.

STEP 4 Formation of fused heterocyclic moiety

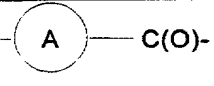
- 15 Each batch of 96 kans was suspended in 5% acetic acid in dioxane (~100 ml) along with the relevant 1,2-diamine (6). The suspensions were then warmed to 80°C with stirring and heated for ~7 h.
- The kans were then filtered and washed with NMP (x2), DCM:DMF 1:1 (x2), methanol (x1), DMA (x2), DCM:DMF 1:1 (x2), DCM (x1), methanol (x2) and ether (x2)(~500 ml each wash). The dried kans were resorted into 8x12 format ready for cleavage.
- 20

STEP 5 Cleavage

- The kans were arranged in cleavage blocks and each was suspended in TFA:DCM:water 16:3:1 (2 ml) and mixed on an orbital shaker for ~1 h. The cleavage solutions were then
- 25 filtered into vials and DCM (1 ml) used to rinse the resin. The combined filtrates were concentrated on a vacuum centrifuge and the desired products isolated by purification using the Parallax HPLC system.

R _s Reagents	Mol. form.	Mol.Wt.	Equivs	Qty (g)
4-AMINO-2,2,6,6-TETRAMETHYLPYPERIDINE	C ₉ H ₂₀ N ₂	156.3	5	5.063
3-DIETHYLAMINOPROPYLAMINE	C ₇ H ₁₈ N ₂	130.2	5	4.220
N,N-DIETHYLETHYLENEDIAMINE	C ₆ H ₁₆ N ₂	116.2	5	3.765
3-AMINOQUINUCLIDINE	C ₇ H ₁₄ N ₂	199.1	5	6.452
N-(3-AMINOPROPYL)MORPHOLINE	C ₇ H ₁₆ N ₂ O	144.2	5	4.673
4-AMINO-1-BENZYLPIPERIDINE	C ₁₂ H ₁₈ N ₂	190.3	5	6.165
1-BOC-4-AMINOPIPERIDINE	C ₅ H ₁₂ N ₂	200.3	5	6.489
3-[4-(3-CHLOROPHENYL)PIPERAZINYL] PROPYLAMINE	C ₁₃ H ₂₀ ClN ₃	253.8	5	8.222
3-[4-(3-CHLORO-6-METHOXYPHENYL)]	C ₁₄ H ₂₂ ClN ₃ O	283.8	5	9.195

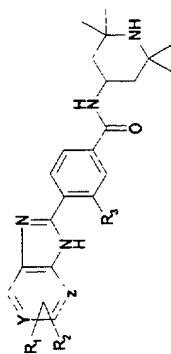
PIPERAZINYL]PROPYLAMINE				
MONO-N-(BOC)-PROPYLENEDIAMINE	C ₃ H ₁₀ N ₂	174.2	5	5.645
3-(AMINOMETHYL)PYRIDINE	C ₆ H ₈ N ₂	108.14	5	3.5

 Reagents	Mol.form.	Mol.Wt.	Equivs	Qty (g)
4-CARBOXYBENZALDEHYDE	C ₈ H ₆ O ₃	150.1	5	4.50
2-METHOXY-4-CARBOXYBENZALDEHYDE	C ₉ H ₈ O ₄	180.2	5	5.40
2-ETHOXY-4-CARBOXYBENZALDEHYDE	C ₁₀ H ₁₀ O ₄	194.2	5	5.82
2-METHYL-4-CARBOXYBENZALDEHYDE	C ₉ H ₈ O ₃	164.2	5	4.92
2-FLUORO-4-CARBOXYBENZALDEHYDE	C ₈ H ₅ FO ₃	168.1	5	5.04
2-BROMO-4-CARBOXYBENZALDEHYDE	C ₈ H ₅ BrO ₃	229.0	5	6.86
5-FORMYL-2-THIOPHENECARBOXYLIC ACID	C ₆ H ₄ O ₃ S	156.2	5	4.68

Fused heterocycle Reagents	Mol.form.	Mol.Wt.	Equivs	Qty (g)
*4-METHOXY-1,2-PHENYLENEDIAMINE	C ₇ H ₉ N ₂ O	139.2	10	5.31
*5-BROMO-3,4-DIMETHYL-1,2-PHENYLENEDIAMINE	C ₈ H ₁₀ BrN ₂	216.1	10	8.26
*5-CHLORO-4-METHYL-1,2-PHENYLENEDIAMINE	C ₇ H ₈ ClN ₂	157.6	10	6.01
*3-METHYL-1,2-PHENYLENEDIAMINE	C ₇ H ₉ N ₂	123.2	10	4.69
*4,5-DICHLORO-1,2-PHENYLENEDIAMINE	C ₆ H ₅ Cl ₂ N ₂	178.0	10	6.80
*4-FLUORO-5-CHLORO-1,2-PHENYLENEDIAMINE	C ₆ H ₅ ClFN ₂	161.6	10	6.17
*3-CHLORO-5-TRIFLUOROMETHYL-1,2-PHENYLENEDIAMINE	C ₇ H ₅ ClF ₃ N ₂	211.6	10	8.09
*2,3-DIAMINONAPHTHALENE	C ₁₀ H ₉ N ₂	159.2	10	6.08
*4-TRIFLUOROMETHYL-1,2-PHENYLENEDIAMINE	C ₇ H ₆ F ₃ N ₂	177.1	10	6.76
*3-HYDROXY-1,2-PHENYLENEDIAMINE	C ₆ H ₇ N ₂ O	125.1	10	4.77
*3,4-DIAMIMOPYRIDINE	C ₅ H ₆ N ₃	110.1	10	4.19
*4,5-DIAMINOPYRIMIDINE	C ₄ H ₅ N ₄	111.1	10	4.23

- 5 The compounds listed in Table 2 were prepared following the procedure described in Example 23, following Preparation 14. All of the library compounds gave the expected [M+H]⁺ pseudomolecular ion signal by mass spectrometry.

Table 2



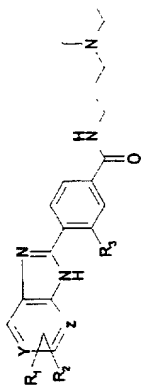
Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
23	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	5-Cl	6-Cl	CH	CH	H
24	4-(6-Methoxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	6-OMe	H	CH	CH	H
25	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	5-Br	6-Me	CH	C(Me)	H
26	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	5-Cl	6-Me	CH	CH	H
27	4-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	4-Me	H	CH	CH	H
28	4-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	7-OH	H	CH	CH	H
29	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	5-Cl	6-F	CH	CH	H
30	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	4-Cl	6-CF ₃	CH	CH	H
31	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
32	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)benzamide	6-CF ₃	H	CH	CH	H
33	4-(6-Methoxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
34	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
35	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
36	4-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	4-Me	H	CH	CH	OMe

Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
37	4-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe
38	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
39	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
40	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe
41	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
42	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	H	H	N	CH	OMe
43	4-(1H-Purin-8-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	H	H	N	N	OMe
44	4-(6-Methoxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methoxybenzamide	6-OMe	H	CH	CH	OEt
45	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
46	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
47	4-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	4-Me	H	CH	CH	OEt
48	4-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
49	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
50	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
51	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OEt
52	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	6-CF ₃	H	CH	CH	OEt
53	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	H	H	N	CH	OEt
54	4-(1H-Purin-8-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-ethoxybenzamide	H	H	N	N	OEt
55	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
56	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
57	4-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	4-Me	H	CH	CH	Me

Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
58	4-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	7-OH	H	CH	CH	Me
59	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
60	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
61	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Me
62	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
63	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	H	H	N	CH	Me
64	4-(1H-Purin-8-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-methylbenzamide	H	H	N	N	Me
65	4-(6-Methoxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	6-OMe	H	CH	CH	F
66	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
67	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
68	4-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	4-Me	H	CH	CH	F
69	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
70	4-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	7-OH	H	CH	CH	F
71	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	5-Cl	6-F	CH	CH	F
72	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
73	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
74	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	6-CF ₃	H	CH	CH	F
75	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-fluorobenzamide	H	H	N	CH	F
76	4-(6-Methoxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	6-OMe	H	CH	CH	Br
77	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br
78	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br

Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
79	4-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	4-Me	H	CH	CH	Br
80	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
81	4-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	7-OH	H	CH	CH	Br
82	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	5-Cl	6-F	CH	CH	Br
83	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	4-Cl	6-CF ₃	CH	CH	Br
84	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br
85	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	6-CF ₃	H	CH	CH	Br
8	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-3-bromobenzamide	H	H	N	CH	Br

Table 2 contd...

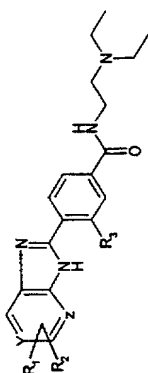


Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
87	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	5-Br	6-Me	CH	C(Me)	H
88	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	5-Cl	6-Me	CH	CH	H
89	4-(4-Methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	4-Me	H	CH	CH	H
90	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	5-Cl	6-Cl	CH	CH	H
91	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	7-OH	H	CH	CH	H
92	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	5-Cl	6-F	CH	CH	H
93	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	4-Cl	6-CF ₃	CH	CH	H
94	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
95	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)benzamide	6-CF ₃	H	CH	CH	H
96	4-(6-Methoxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
97	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
98	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
99	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
100	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe
101	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
102	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
103	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe

104	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
105	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	H	H	N	CH	OMe
106	4-(1H-Purin-8-yl)-N-(3-diethylaminopropyl)-3-methoxybenzamide	H	H	N	N	OMe
107	4-(6-Methoxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	6-OMe	H	CH	CH	OEt
108	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
109	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
110	4-(4-Methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	4-Me	H	CH	CH	OEt
111	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
112	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
113	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
114	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
115	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)	5,6(-CH=CH-CH=CH-)	CH	CH	OEt
116	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	6-CF ₃	H	CH	CH	OEt
117	4-(1H-Purin-8-yl)-N-(3-diethylaminopropyl)-3-ethoxybenzamide	H	H	N	N	OEt
118	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
119	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
120	4-(4-Methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	4-Me	H	CH	CH	Me
121	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
122	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	7-OH	H	CH	CH	Me
123	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
124	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
125	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)	5,6(-CH=CH-CH=CH-)	CH	CH	Me

126	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
127	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	H	H	N	CH	Me
128	4-(1H-Purin-8-yl)-N-(3-diethylaminopropyl)-3-methylbenzamide	H	H	N	N	Me
12	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
130	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
131	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
132	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-fluorobenzamide	5-Cl	6-F	CH	CH	F
133	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
134	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br
135	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br
136	4-(4-Methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	4-Me	H	CH	CH	Br
137	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	5-Cl	6-F	CH	CH	Br
138	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br
139	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	6-CF ₃	H	CH	CH	Br
140	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	H	H	N	CH	Br
141	4-(1H-Purin-8-yl)-N-(3-diethylaminopropyl)-3-bromobenzamide	H	H	N	N	Br

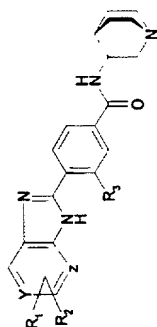
Table 2 contd....



Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
142	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)benzamide	5-Br	6-Me	CH	C(Me)	H
143	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)benzamide	5-Cl	6-Cl	CH	CH	H
144	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)benzamide	6-CF ₃	H	CH	CH	H
145	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
146	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe
147	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
148	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
149	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
150	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
151	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
152	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
153	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
154	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
155	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
156	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
157	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
158	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	7-OH	H	CH	CH	Me

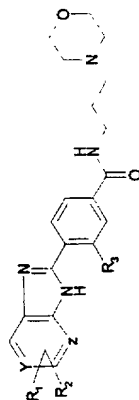
159	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
160	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
161	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	5,8(-CH=CH-CH=CH-)		CH	CH	Me
162	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-3-methylbenzamide	6-CF ₃	H	CH	CH	Me

Table 2 contd...



Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
163	4-(6-Methoxybenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)benzamide	6-OMe	H	CH	CH	H
164	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)benzamide	5-Cl	6-Cl	CH	CH	H
165	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
166	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe
167	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
168	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OEt
169	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-methylbenzamide	7-OH	H	CH	CH	Me
170	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
171	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Me
172	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
173	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
174	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br

Table 2 contd....

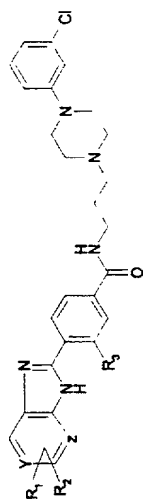


Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
175	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	6-OMe	H	CH	CH	H
176	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	5-Br	6-Me	CH	C(Me)	H
177	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	5-Cl	6-Me	CH	CH	H
178	4-(4-Methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	4-Me	H	CH	CH	H
179	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	5-Cl	6-Cl	CH	CH	H
180	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	7-OH	H	CH	CH	H
181	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	5-Cl	6-F	CH	CH	H
182	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	4-Cl	6-CF ₃	CH	CH	H
183	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
184	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]benzamide	6-CF ₃	H	CH	CH	H
185	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
186	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
187	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
188	4-(4-Methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	4-Me	H	CH	CH	OMe
189	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
190	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	7-OH	H	CH	CH	OMe
191	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
192	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe

193	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	OMe
194	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	6-CF ₃	CH	CH	OMe
195	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-(morpholino)propyl]-3-methoxybenzamide	H	N	CH	OMe
196	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	6-OMe	CH	CH	OEt
197	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	5-Br	CH	C(Me)	OEt
198	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	5-Cl	CH	CH	OEt
199	4-(4-Methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	4-Me	CH	CH	OEt
200	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	5-Cl	CH	CH	OEt
201	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	7-OH	CH	CH	OEt
202	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	5-Cl	CH	CH	OEt
203	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	4-Cl	CH	CH	OEt
204	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	OEt
205	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	6-CF ₃	CH	CH	OEt
206	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	H	N	CH	OEt
207	4-(1H-Purin-8-yl)-N-[3-(morpholino)propyl]-3-ethoxybenzamide	H	N	N	OEt
208	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	6-OMe	CH	CH	Me
209	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	5-Br	CH	C(Me)	Me
210	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	5-Cl	CH	CH	Me
211	4-(4-Methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	4-Me	CH	CH	Me
212	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	5-Cl	CH	CH	Me
213	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	7-OH	CH	CH	Me
214	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	5-Cl	CH	CH	Me
215	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	4-Cl	CH	CH	Me

216	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	Me
217	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	6-CF ₃	H	CH	Me
218	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	H	H	N	Me
219	4-(1H-Purin-8-yl)-N-[3-(morpholino)propyl]-3-methylbenzamide	H	H	N	Me
220	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	6-OMe	H	CH	F
221	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	5-Br	6-Me	CH	F
222	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	5-Cl	6-Me	CH	F
223	4-(4-Methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	4-Me	H	CH	F
224	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	5-Cl	6-Cl	CH	F
225	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	5-Cl	6-F	CH	F
226	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	4-Cl	6-CF ₃	CH	F
227	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	F
228	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	6-CF ₃	H	CH	F
229	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-(morpholino)propyl]-3-fluorobenzamide	H	H	N	F
230	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	6-OMe	H	CH	Br
231	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	5-Br	6-Me	CH	Br
232	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	5-Cl	6-Me	CH	Br
233	4-(4-Methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	4-Me	H	CH	Br
234	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	5-Cl	6-Cl	CH	Br
235	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	5-Cl	6-F	CH	Br
236	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	4-Cl	6-CF ₃	CH	Br
237	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-3-bromobenzamide	6-CF ₃	H	CH	Br

Table 2 contd....



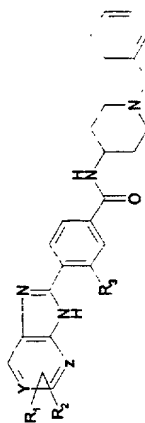
Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
238	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	6-OMe	H	CH	CH	H
239	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	5-Br	6-Me	CH	C(Me)	H
240	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	5-Cl	6-Me	CH	CH	H
241	4-(4-Methylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	4-Me	H	CH	CH	H
242	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	5-Cl	6-Cl	CH	CH	H
243	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	7-OH	H	CH	CH	H
244	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	5-Cl	6-F	CH	CH	H
245	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	4-Cl	6-CF ₃	CH	CH	H
246	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	5,6(-CH=CH-CH=CH-)	CH	CH	CH	H
247	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	6-CF ₃	H	CH	CH	H
248	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	H	H	N	CH	H
249	4-(1H-Purin-8-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]benzamide	H	H	N	N	H
250	4-(6-Methoxybenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
251	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
252	4-(4-Methylbenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]-3-methoxybenzamide	4-Me	H	CH	CH	OMe
253	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
254	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-(4-(3-chlorophenyl)piperazinyl)propyl]-3-methoxybenzamide	7-OH	H	CH	CH	OMe

255	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
256	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
257	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe
258	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
259	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	H	H	N	CH	OMe
260	4-(1H-Purin-8-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	H	H	N	N	OMe
261	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	6-OMe	H	CH	CH	OEt
262	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
263	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
264	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	4-Me	H	CH	CH	OEt
265	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
266	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
267	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
268	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
269	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OEt
270	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	6-CF ₃	H	CH	CH	OEt
271	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	H	H	N	CH	OEt
272	4-(1H-Purin-8-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	H	H	N	N	OEt
273	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	6-OMe	H	CH	CH	Me
274	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
275	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me

276	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	4-Me	H	CH	CH	Me
277	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
278	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	7-OH	H	CH	CH	Me
279	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
280	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
281	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Me
282	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
283	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	H	H	N	CH	Me
284	4-(1H-Purin-8-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	H	H	N	N	Me
285	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	6-OMe	H	CH	CH	F
286	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
287	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
288	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	4-Me	H	CH	CH	F
289	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
290	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	7-OH	H	CH	CH	F
291	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Cl	6-F	CH	CH	F
292	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
293	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
294	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	6-CF ₃	H	CH	CH	F
295	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	H	H	N	CH	F
296	4-(1H-Purin-8-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	H	H	N	N	F

297	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	6-OMe	H	CH	CH	Br
298	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br
299	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br
300	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	4-Me	H	CH	CH	Br
301	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
302	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	7-OH	H	CH	CH	Br
303	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Cl	6-F	CH	CH	Br
304	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	4-Cl	6-CF ₃	CH	CH	Br
305	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br
306	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	6-CF ₃	H	CH	CH	Br
307	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	H	H	N	CH	Br
308	4-(1H-Purin-8-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	H	H	N	N	Br

Table 2 contd...



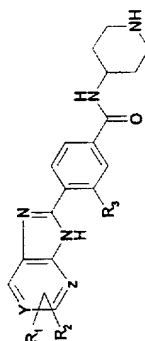
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309	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	5-Br	6-Me	CH	C(Me)	H
310	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	5-Cl	6-Me	CH	CH	H
311	4-(4-Methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	4-Me	H	CH	CH	H
312	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	5-Cl	6-Cl	CH	CH	H
313	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	7-OH	H	CH	CH	H
314	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	5-Cl	6-F	CH	CH	H
315	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	4-Cl	6-CF ₃	CH	CH	H
316	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
317	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	6-CF ₃	H	CH	CH	H
318	4-(1H-imidazol[4,5-b]pyridin-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	H	H	N	CH	H
319	4-(1H-Purin-8-yl)-N-(1-phenylmethylpiperidinyl-4-yl)benzamide	H	H	N	N	H
320	4-(6-Methoxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
321	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
322	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
323	4-(4-Methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	4-Me	H	CH	CH	OMe
324	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
325	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe

326	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
327	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
328	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe
329	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
330	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	H	H	N	CH	OMe
331	4-(1H-Purin-8-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methoxybenzamide	H	H	N	N	OMe
332	4-(6-Methoxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	6-OMe	H	CH	CH	OEt
333	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
334	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
335	4-(4-Methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	4-Me	H	CH	CH	OEt
336	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
337	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
338	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
339	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
340	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OEt
341	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	6-CF ₃	H	CH	CH	OEt
342	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	H	H	N	CH	OEt
343	4-(1H-Purin-8-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-ethoxybenzamide	H	H	N	N	OEt
344	4-(6-Methoxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	6-OMe	H	CH	CH	Me
345	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
346	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
347	4-(4-Methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	4-Me	H	CH	CH	Me

348	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
349	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	7-OH	H	CH	CH	Me
350	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
351	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
352	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Me
353	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
354	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	H	H	N	CH	Me
355	4-(1H-Purin-8-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-methylbenzamide	H	H	N	N	Me
356	4-(6-Methoxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	6-OMe	H	CH	CH	F
357	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
358	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
359	4-(4-Methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	4-Me	H	CH	CH	F
360	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
361	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	7-OH	H	CH	CH	F
362	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	5-Cl	6-F	CH	CH	F
363	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
364	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
365	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	6-CF ₃	H	CH	CH	F
366	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	H	H	N	CH	F
367	4-(1H-Purin-8-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-fluorobenzamide	H	H	N	N	F
368	4-(6-Methoxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	6-OMe	H	CH	CH	Br
369	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br

370	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br
371	4-(4-Methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	4-Me	H	CH	CH	Br
372	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
373	4-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	7-OH	H	CH	CH	Br
374	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	4-Cl	6-CF ₃	CH	CH	Br
375	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	5,6-(CH=CH-CH=CH-)		CH	CH	Br
376	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	6-CF ₃	H	CH	CH	Br
377	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	H	H	N	CH	Br
378	4-(1H-Purin-8-yl)-N-(1-phenylmethylpiperidinyl-4-yl)-3-bromobenzamide	H	H	N	N	Br

Table 2 contd...



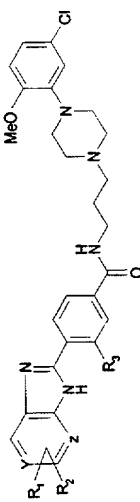
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379	4-(6-Methoxybenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	6-OMe	H	CH	CH	H
380	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	5-Br	6-Me	CH	C(Me)	H
381	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	5-Cl	6-Me	CH	CH	H
382	4-(4-Methylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	4-Me	H	CH	CH	H
383	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	5-Cl	6-Cl	CH	CH	H
384	4-(7-Hydroxybenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	7-OH	H	CH	CH	H
385	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	5-Cl	6-F	CH	CH	H
386	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	4-Cl	6-CF ₃	CH	CH	H
387	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidinyl-4-yl)benzamide	5,6-(CH=CH-CH=CH-)		CH	CH	H

388	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)benzamide	6-CF ₃	H	CH	CH	H
389	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidin-4-yl)benzamide	H	H	N	CH	H
390	4-(1H-Purin-8-yl)-N-(piperidin-4-yl)benzamide	H	H	N	N	H
391	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
392	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
393	4-(4-Methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	4-Me	H	CH	CH	OMe
394	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
395	4-(7-Hydroxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe
396	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
397	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
398	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe
399	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
400	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	H	H	N	CH	OMe
401	4-(1H-Purin-8-yl)-N-(piperidin-4-yl)-3-methoxybenzamide	H	H	N	N	OMe
402	4-(6-Methoxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	6-OMe	H	CH	CH	OEt
403	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
404	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
405	4-(4-Methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	4-Me	H	CH	CH	OEt
406	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
407	4-(7-Hydroxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
408	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
409	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
410	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OEt
411	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	6-CF ₃	H	CH	CH	OEt

412	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	H	H	N	CH	OEt
413	4-(1H-Purin-8-yl)-N-(piperidin-4-yl)-3-ethoxybenzamide	H	H	N	N	OEt
414	4-(6-Methoxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	6-OMe	H	CH	CH	Me
415	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
416	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
417	4-(4-Methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	4-Me	H	CH	CH	Me
418	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
419	4-(7-Hydroxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	7-OH	H	CH	CH	Me
420	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
421	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
422	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Me
423	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
424	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidin-4-yl)-3-methylbenzamide	H	H	N	CH	Me
425	4-(6-Methoxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	6-OMe	H	CH	CH	F
426	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
427	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
428	4-(4-Methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	4-Me	H	CH	CH	F
429	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
430	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	5-Cl	6-F	CH	CH	F
431	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
432	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
433	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	6-CF ₃	H	CH	CH	F
434	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidin-4-yl)-3-fluorobenzamide	H	H	N	CH	F
435	4-(6-Methoxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	6-OMe	H	CH	CH	Br

436	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br
437	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br
438	4-(4-Methylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	4-Me	H	CH	CH	Br
439	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
440	4-(7-Hydroxybenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	7-OH	H	CH	CH	Br
441	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	5-Cl	6-F	CH	CH	Br
442	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	4-Cl	6-CF ₃	CH	CH	Br
443	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br
444	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	6-CF ₃	H	CH	CH	Br
445	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidin-4-yl)-3-bromobenzamide	H	H	N	CH	Br

Table 2 contd...



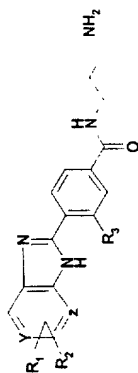
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446	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	6-OMe	H	CH	CH	H
447	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	5-Br	6-Me	CH	C(Me)	H
448	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	5-Cl	6-Me	CH	CH	H
449	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	4-Me	H	CH	CH	H
450	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	5-Cl	6-Cl	CH	CH	H
451	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	7-OH	H	CH	CH	H
452	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	5-Cl	6-F	CH	CH	H

453	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	4-Cl	6-CF ₃	CH	CH	H
454	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
455	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	6-CF ₃	H	CH	CH	H
456	4-(1H-Purin-8-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]benzamide	H	H	N	N	H
457	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
458	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
459	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	4-Me	H	CH	CH	OMe
460	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
461	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	7-OH	H	CH	CH	OMe
462	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
463	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
464	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	OMe
465	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
466	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	H	H	N	CH	OMe
467	4-(1H-Purin-8-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methoxybenzamide	H	H	N	N	OMe
468	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	6-OMe	H	CH	CH	OEt
469	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
470	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
471	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
472	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
473	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt

474	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
475	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	5,6-(CH=CH-CH=CH-)		CH	CH	OEt
476	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	H	H	N	CH	OEt
477	4-(1H-Purin-8-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-ethoxybenzamide	H	H	N	N	OEt
478	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	6-OMe	H	CH	CH	Me
479	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
480	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
481	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
482	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	7-OH	H	CH	CH	Me
483	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
484	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me
485	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
486	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	H	H	N	CH	Me
487	4-(1H-Purin-8-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-methylbenzamide	H	H	N	N	Me
488	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	6-OMe	H	CH	CH	F
489	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
490	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
491	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	4-Me	H	CH	CH	F
492	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
493	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	7-OH	H	CH	CH	F
494	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5-Cl	6-F	CH	CH	F

495	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
496	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
497	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	6-CF ₃	H	CH	CH	F
498	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	H	H	N	CH	F
499	4-(1H-Purin-8-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-fluorobenzamide	H	H	N	N	F
500	4-(6-Methoxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	6-OMe	H	CH	CH	Br
501	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br
502	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br
503	4-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	4-Me	H	CH	CH	Br
504	4-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
505	4-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	7-OH	H	CH	CH	Br
506	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5-Cl	6-F	CH	CH	Br
507	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	4-Cl	6-CF ₃	CH	CH	Br
508	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br
509	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	6-CF ₃	H	CH	CH	Br
510	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	H	H	N	CH	Br
511	4-(1H-Purin-8-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-3-bromobenzamide	H	H	N	N	Br

Table 2 contd...

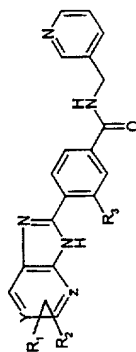


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512	4-(6-Methoxybenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	6-OMe	H	CH	CH	H
513	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	5-Br	6-Me	CH	C(Me)	H
514	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	5-Cl	6-Me	CH	CH	H
515	4-(4-Methylbenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	4-Me	H	CH	CH	H
516	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	5-Cl	6-Cl	CH	CH	H
517	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	7-OH	H	CH	CH	H
518	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	5-Cl	6-F	CH	CH	H
519	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	4-Cl	6-CF ₃	CH	CH	H
520	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-aminopropyl)benzamide	5,6-(CH=CH-CH=CH-)		CH	CH	H
521	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)benzamide	6-CF ₃	H	CH	CH	H
522	4-(6-Methoxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
523	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
524	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
525	4-(4-Methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	4-Me	H	CH	CH	OMe
526	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
527	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe
528	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe

529	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe
530	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	5,6-(CH=CH-CH=CH-)		CH	CH	OMe
531	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methoxybenzamide	6-CF ₃	H	CH	CH	OMe
532	4-(1H-Purin-8-yl)-N-(3-aminopropyl)-3-methoxybenzamide	H	H	N	N	OMe
533	4-(6-Methoxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	6-OMe	H	CH	CH	OEt
534	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	5-Br	6-Me	CH	C(Me)	OEt
535	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	5-Cl	6-Me	CH	CH	OEt
536	4-(4-Methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	4-Me	H	CH	CH	OEt
537	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	5-Cl	6-Cl	CH	CH	OEt
538	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	7-OH	H	CH	CH	OEt
539	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	5-Cl	6-F	CH	CH	OEt
540	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	4-Cl	6-CF ₃	CH	CH	OEt
541	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	5,6-(CH=CH-CH=CH-)		CH	CH	OEt
542	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	6-CF ₃	H	CH	CH	OEt
543	4-(1H-Imidazol-4,5-bipyridin-2-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	H	H	N	CH	OEt
544	4-(1H-Purin-8-yl)-N-(3-aminopropyl)-3-ethoxybenzamide	H	H	N	N	OEt
545	4-(6-Methoxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	6-OMe	H	CH	CH	Me
546	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	5-Br	6-Me	CH	C(Me)	Me
547	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	5-Cl	6-Me	CH	CH	Me
548	4-(4-Methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	4-Me	H	CH	CH	Me
549	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	5-Cl	6-Cl	CH	CH	Me
550	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	7-OH	H	CH	CH	Me
551	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	5-Cl	6-F	CH	CH	Me
552	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	4-Cl	6-CF ₃	CH	CH	Me

553	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	Me
554	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-methylbenzamide	6-CF ₃	H	CH	Me
555	4-(6-Methoxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	6-OMe	H	CH	F
556	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	5-Br	6-Me	CH	F
557	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	5-Cl	6-Me	CH	F
558	4-(4-Methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	4-Me	H	CH	F
559	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	5-Cl	6-Cl	CH	F
560	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	7-OH	H	CH	F
561	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	5-Cl	6-F	CH	F
562	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	4-Cl	6-CF ₃	CH	F
563	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	F
564	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-fluorobenzamide	6-CF ₃	H	CH	F
565	4-(6-Methoxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	6-OMe	H	CH	Br
566	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	5-Br	6-Me	CH	Br
567	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	5-Cl	6-Me	CH	Br
568	4-(4-Methylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	4-Me	H	CH	Br
569	4-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	5-Cl	6-Cl	CH	Br
570	4-(7-Hydroxybenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	7-OH	H	CH	Br
571	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	5-Cl	6-F	CH	Br
572	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	4-Cl	6-CF ₃	CH	Br
573	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	Br
574	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-aminopropyl)-3-bromobenzamide	6-CF ₃	H	CH	Br

Table 2 contd. ...

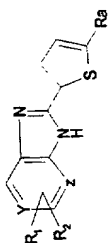


Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
575	4-(6-Methoxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	6-OMe	H	CH	CH	H
576	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	5-Br	6-Me	CH	C(Me)	H
577	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	5-Cl	6-Me	CH	CH	H
578	4-(4-Methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	4-Me	H	CH	CH	H
579	4-(5,6-Dichlorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	5-Cl	6-Cl	CH	CH	H
580	4-(7-Hydroxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	7-OH	H	CH	CH	H
581	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	5-Cl	6-F	CH	CH	H
582	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	4-Cl	6-CF ₃	CH	CH	H
583	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	5,6(-CH=CH-CH=CH-)		CH	CH	H
584	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)benzamide	6-CF ₃	H	CH	CH	H
585	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-((piridin-3-yl)methyl)benzamide	H	H	N	CH	H
586	4-(6-Methoxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	6-OMe	H	CH	CH	OMe
587	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	5-Br	6-Me	CH	C(Me)	OMe
588	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	5-Cl	6-Me	CH	CH	OMe
589	4-(4-Methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	4-Me	H	CH	CH	OMe
590	4-(5,6-Dichlorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	5-Cl	6-Cl	CH	CH	OMe
591	4-(7-Hydroxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	7-OH	H	CH	CH	OMe
592	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	5-Cl	6-F	CH	CH	OMe
593	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	4-Cl	6-CF ₃	CH	CH	OMe

594	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	OMe
595	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	6-CF ₃	CH	CH	OMe
596	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-((piridin-3-yl)methyl)-3-methoxybenzamide	H	N	CH	OMe
597	4-(6-Methoxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	6-OMe	CH	CH	OEt
598	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	5-Br	CH	C(Me)	OEt
599	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	5-Cl	CH	CH	OEt
600	4-(4-Methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	4-Me	CH	CH	OEt
601	4-(5,6-Dichlorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	5-Cl	CH	CH	OEt
602	4-(7-Hydroxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	7-OH	CH	CH	OEt
603	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	5-Cl	CH	CH	OEt
604	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	4-Cl	CH	CH	OEt
605	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	OEt
606	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	6-CF ₃	CH	CH	OEt
607	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-((piridin-3-yl)methyl)-3-ethoxybenzamide	H	N	CH	OEt
608	4-(6-Methoxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	6-OMe	CH	CH	Me
609	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	5-Br	CH	C(Me)	Me
610	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	5-Cl	CH	CH	Me
611	4-(4-Methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	4-Me	CH	CH	Me
612	4-(5,6-Dichlorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	5-Cl	CH	CH	Me
613	4-(7-Hydroxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	7-OH	CH	CH	Me
614	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	5-Cl	CH	CH	Me
615	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	4-Cl	CH	CH	Me
616	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	5,6(-CH=CH-CH=CH-)	CH	CH	Me

617	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	6-CF ₃	H	CH	CH	Me
618	4-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-((piridin-3-yl)methyl)-3-methylbenzamide	H	H	N	CH	Me
619	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	5-Br	6-Me	CH	C(Me)	F
620	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	5-Cl	6-Me	CH	CH	F
621	4-(4-Methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	4-Me	H	CH	CH	F
622	4-(5,6-Dichlorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	5-Cl	6-Cl	CH	CH	F
623	4-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	5-Cl	6-F	CH	CH	F
624	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	4-Cl	6-CF ₃	CH	CH	F
625	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	F
626	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-fluorobenzamide	6-CF ₃	H	CH	CH	F
627	4-(6-Methoxybenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	6-OMe	H	CH	CH	Br
628	4-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	5-Br	6-Me	CH	C(Me)	Br
629	4-(5-Chloro-6-methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	5-Cl	6-Me	CH	CH	Br
630	4-(4-Methylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	4-Me	H	CH	CH	Br
631	4-(5,6-Dichlorobenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	5-Cl	6-Cl	CH	CH	Br
632	4-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	4-Cl	6-CF ₃	CH	CH	Br
633	4-(1H-Naphth[2,3-d]imidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	5,6(-CH=CH-CH=CH-)		CH	CH	Br
634	4-(6-Trifluoromethylbenzimidazol-2-yl)-N-((piridin-3-yl)methyl)-3-bromobenzamide	6-CF ₃	H	CH	CH	Br

Tabel 2 contd...

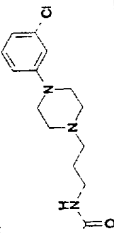
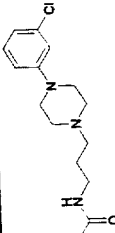
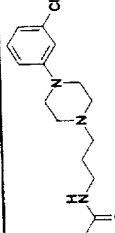
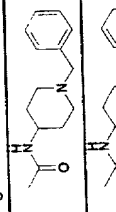
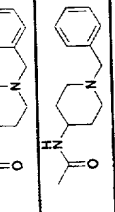
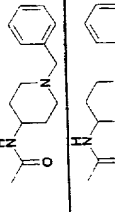
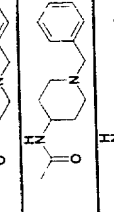
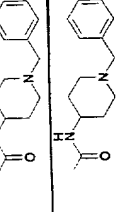
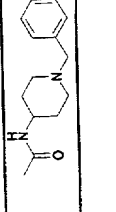





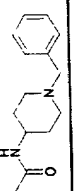

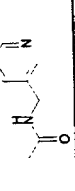
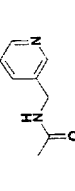

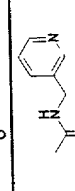
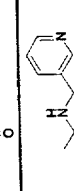
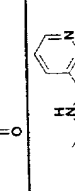
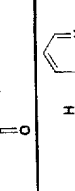
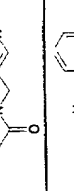
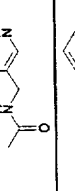
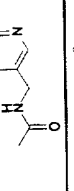
Ex. No	Name	R ₁	R ₂	Y	Z	R ₃
635	5-(6-Methoxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	6-OMe	H	CH	CH	
636	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	5-Br	6-Me	CH	C(Me)	
637	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	5-Cl	6-Me	CH	CH	
638	5-(4-Methylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	4-Me	H	CH	CH	
639	5-(5,6-Dichlorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	5-Cl	6-Cl	CH	CH	
640	5-(7-Hydroxybenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	7-OH	H	CH	CH	
641	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	5-Cl	6-F	CH	CH	
642	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	4-Cl	6-CF ₃	CH	CH	
643	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	5,6-(CH=CH-CH=CH-)		CH	CH	

644	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	6-CF ₃	H	CH	CH	
645	5-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(2,2,6,6-tetramethylpiperidin-4-yl)-2-thiophenamide	H	H	N	CH	
646	5-(6-Methoxybenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	6-OMe	H	CH	CH	
647	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	5-Br	6-Me	CH	C(Me)	
648	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	5-Cl	6-Me	CH	CH	
649	5-(4-Methylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	4-Me	H	CH	CH	
650	5-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	5-Cl	6-Cl	CH	CH	
651	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	5-Cl	6-F	CH	CH	
652	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	5,6(-CH=CH-CH=CH-)		CH	CH	
653	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminopropyl)-2-thiophenamide	6-CF ₃	H	CH	CH	
654	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-2-thiophenamide	5-Br	6-Me	CH	C(Me)	
655	5-(5,6-Dichlorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-2-thiophenamide	5-Cl	6-Cl	CH	CH	

656	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(3-diethylaminoethyl)-2-thiophenamide	5-Cl	6-F	CH	CH	
657	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-2-thiophenamide	4-Cl	6-CF ₃	CH	CH	
658	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(3-diethylaminoethyl)-2-thiophenamide	5,6(-CH=CH-CH=CH-)		CH	CH	
659	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-(3-diethylaminoethyl)-2-thiophenamide	6-CF ₃	H	CH	CH	
660	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-2-thiophenamide	5,6(-CH=CH-CH=CH-)		CH	CH	
661	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-azabicyclo[2.2.2]octan-3-yl)-2-thiophenamide	6-CF ₃	H	CH	CH	
662	5-(6-Methoxybenzimidazol-2-yl)-N-(3-(morpholino)propyl)-2-thiophenamide	6-OMe	H	CH	CH	
663	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	5-Br	6-Me	CH	C(Me)	
664	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	5-Cl	6-Me	CH	CH	
665	5-(4-Methylbenzimidazol-2-yl)-N-(3-(morpholino)propyl)-2-thiophenamide	4-Me	H	CH	CH	
666	5-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	5-Cl	6-Cl	CH	CH	
667	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	5-Cl	6-F	CH	CH	
668	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	4-Cl	6-CF ₃	CH	CH	

669	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	5,6(-CH=CH-CH=CH-)	CH	CH	
670	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-(morpholino)propyl]-2-thiophenamide	6-CF ₃	CH	CH	
671	5-(6-Methoxybenzimidazol-2-yl)-N-[3-(4-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	6-OMe	CH	CH	
672	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5-Cl	CH	CH	
673	5-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	4-Me	CH	CH	
674	5-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5-Cl	CH	CH	
675	5-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	7-OH	CH	CH	
676	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5-Cl	CH	CH	
677	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	4-Cl	CH	CH	

678	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5,6(-CH=CH-CH=CH-)	CH	CH	
679	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	6-CF ₃	H	CH	
680	5-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[3-[4-(3-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	H	H	N	
681	5-(6-Methoxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	6-OMe	H	CH	
682	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	5-Br	6-Me	CH	
683	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	5-Cl	6-Me	CH	
684	5-(5,6-Dichlorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	5-Cl	6-Cl	CH	
685	5-(7-Hydroxybenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	7-OH	H	CH	
686	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	5-Cl	6-F	CH	
687	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	4-Cl	6-CF ₃	CH	
688	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	5,6(-CH=CH-CH=CH-)		CH	
689	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-(1-phenylmethylpiperidin-4-yl)-2-thiophenamide	6-CF ₃	H	CH	

690	5-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(1-phenylmethyl)piperidin-4-yl)-2-thiophenamide	H	H	N	CH	
691	5-(1H-Purin-8-yl)-N-(1-phenylmethyl)piperidin-4-yl)-2-thiophenamide	H	H	N	N	
692	5-(6-Methoxybenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	6-OMe	H	CH	CH	
693	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	5-Br	6-Me	CH	C(Me)	
694	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	5-Cl	6-Me	CH	CH	
695	5-(4-Methylbenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	4-Me	H	CH	CH	
696	5-(5,6-Dichlorobenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	5-Cl	6-Cl	CH	CH	
697	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	5-Cl	6-F	CH	CH	
698	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	4-Cl	6-CF ₃	CH	CH	
699	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	5,6(-CH=CH-CH=CH-)		CH	CH	
700	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	6-CF ₃	H	CH	CH	
701	5-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-[(3-pyridyl)methyl]-2-thiophenamide	H	H	N	CH	

702	5-(6-Methoxybenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	6-OMe	H	CH	CH	
703	5-(5-Bromo-6,7-dimethylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	5-Br	6-Me	CH	CH	
704	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	5-Cl	6-Me	CH	CH	
705	5-(4-Methylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	4-Me	H	CH	CH	
706	5-(5,6-Dichlorobenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	5-Cl	6-Cl	CH	CH	
707	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	5-Cl	6-F	CH	CH	
708	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	4-Cl	6-CF ₃	CH	CH	
709	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	5,6(-CH=CH-CH=CH-)		CH	CH	
710	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	6-CF ₃	H	CH	CH	
711	5-(1H-Imidazo[4,5-b]pyridin-2-yl)-N-(piperidinyl-4-yl)-2-thiophenamide	H	H	N	CH	
712	5-(6-Methoxybenzimidazol-2-yl)-N-[3-(4-methoxy-5-chlorophenyl)piperazinyl]propyl-2-thiophenamide	6-OMe	H	CH	CH	
713	5-(5-Chloro-6-methylbenzimidazol-2-yl)-N-[3-(4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl-2-thiophenamide	5-Cl	6-Me	CH	CH	

714	5-(4-Methylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	4-Me	H	CH	CH	
715	5-(5,6-Dichlorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5-Cl	6-Cl	CH	CH	
716	5-(7-Hydroxybenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	7-OH	H	CH	CH	
717	5-(5-Chloro-6-fluorobenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5-Cl	6-F	CH	CH	
718	5-(4-Chloro-6-trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	4-Cl	6-CF ₃	CH	CH	
719	5-(1H-Naphth[2,3-d]imidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	5,6-(CH=CH-CH=CH-)		CH	CH	
720	5-(6-Trifluoromethylbenzimidazol-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	6-CF ₃	H	CH	CH	
721	5-(1H-Imidazol[4,5-b]pyridin-2-yl)-N-[3-[4-(2-methoxy-5-chlorophenyl)piperazinyl]propyl]-2-thiophenamide	H	H	N	CH	

Biological Assays

Background. It is known that, upon attachment to bone, an electrogenic H^+ - adenosine triphosphatase (ATPase) is polarised to the osteoclast-bone interface. The pump transports massive quantities of protons into the resorption microenvironment to effect mobilisation of the bone mineral and to create the acidic pH required by collagenases to degrade the bone matrix.

The vacuolar nature of the osteoclast proton pump was originally recognised by Blair [H. C. Blair et al., *Science*, 245, 855 (1989)] and then confirmed by Bekker [P.J. Bekker et al., *J. Bone Min. Res.*, 5, 569 (1990)] and Väänänen [H.K. Väänänen et al., *J. Cell. Biol.*, 111, 1305 (1990)]. Evidence was based upon preparations of ruffled membrane fragments from avian osteoclasts (obtained from the medullar bone of calcium-starved egg-laying hens). The resulting membrane vesicles acidify in response to ATP, which is easily assessed by measuring the fluorescence quench of acridine orange, a weak base which accumulates into acidic compartments.

The biochemical pattern indicated that the osteoclast proton pump belonged to the vacuolar-like ATPases since proton transport was inhibited by N-ethylmaleimide (NEM), a sulphydryl reagent, and by bafilomycin A_1 , a selective inhibitor of vacuolar H^+ - ATPases [J.E. Bowman et al., *Proc. Natl. Acad. Sci. USA*, 85, 7972 (1988)], whilst it was not inhibited by ouabain, an inhibitor of Na^+/K^+ -ATPases; sodium orthovanadate, an inhibitor of P-ATPases, or by omeprazole or SCH 28080, both of which are inhibitors of gastric H^+/K^+ -ATPase [J.P. Mattsson et al., *Acta Physiol. Scand.*, 146, 253 (1992)].

It is known that specific inhibitors of vacuolar ATPases, such as bafilomycin A_1 , are able to inhibit bone resorption in osteoclast cultures [K. Sundquist et al., *Biochem. Biophys. Res. Commun.* 168, 309-313 (1990)]

Inhibition Of Proton Transport And v-ATPase Activity In Membrane Vesicles

Preparation of human osteoclast microsomal vesicles. Osteoclast-like giant cells isolated from osteoclastoma tumor were homogenized with a glass-teflon homogenizer (1000 rpm x 20 strokes), and the material was centrifuged at 6000 x gmax for 20 minutes. The resulting pellet was then spun at 100000 x gmax for 60 minutes to pellet the microsomal fraction. Resuspended in 1 ml of isolation medium pH 7.4, frozen by liquid nitrogen immersion and stored at -80°C until used.

Proton transport in membrane vesicles was assessed, semi-quantitatively, by measuring the initial slope of fluorescence quench of acridine orange (excitation 490 nm; emission 530 nm) after addition of 5-20 μl of membrane vesicles in 1 ml of buffer containing 0.2 M sucrose, 50 mM KCl, 10 mM Hepes pH 7.4, 1 mM ATP.Na2, 1 mM CDTA, 5 μM valinomycin and 4 μM acridine orange. The reaction was started by addition of 5 mM MgSO_4 . Results were expressed as the percent of the mean of two controls.

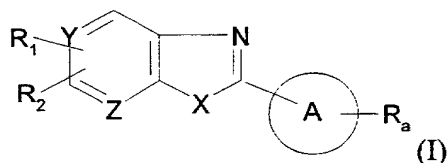
- Inhibition of bafilomycin-sensitive ATPase activity** was assessed in purified membrane vesicles by measuring the release of inorganic phosphate (Pi) during 30 min of incubation at 37°C in a 96-well plate either in the presence or in the absence of bafilomycin A1. The reaction medium contained 1 mM ATP, 10 mM HEPES-Tris pH 8, 50 mM KCl, 5 uM valinomycin, 5 uM nigericin, 1 mM CDTA-Tris, 100 uM ammonium molybdate, 0.2 M sucrose and membranes (20 ug protein/ml). The reaction was initiated by MgSO₄ (8-arm pipette) and stopped, after 30 min, by addition of 4 volumes of the malachite green reagent (96-arm pipette) prepared according to Chan [*Anal. Biochem.* 157, 375 (1986)]. Absorbance at 650 nm was measured after 2 min using a microplate reader. Results are expressed as nmol (Pi) × mg protein⁻¹ × min⁻¹ and, for each experiment, represent the mean ± sem of triplicates.

Pharmacological Data

- Compounds described in the present invention are able to inhibit bafilomycin-sensitive ATPase of human osteoclasts in a range from 2 nM to 15 µM.

Claims

A compound of formula (I)



or a salt thereof, or a solvate thereof, wherein;

X represents oxygen, sulphur, or NR_b , wherein R_b represents hydrogen, unsubstituted or substituted C_{1-6} alkyl or unsubstituted or substituted C_{1-6} alkylcarbonyl;

Y and Z each independently represent nitrogen, CH, CR_1 or CR_2 ;

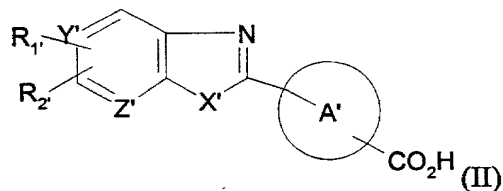
A represents an unsubstituted or substituted aryl group or an unsubstituted or substituted heterocyclyl group;

R_a represents $-\text{C}(\text{O})\text{NR}_s\text{R}_t$ wherein R_s and R_t each independently represent hydrogen, unsubstituted or substituted C_{1-6} alkyl, unsubstituted or substituted C_3 -gycycloalkyl, unsubstituted or substituted C_{1-6} alkenyl, unsubstituted or substituted aryl, unsubstituted or substituted aryl C_{1-6} alkyl, unsubstituted or substituted heterocyclyl or an unsubstituted or substituted heterocyclyl C_{1-6} alkyl group, or R_s and R_t together with the nitrogen to which they are attached form a heterocyclyl group;

R_1 and R_2 each independently represents hydrogen, hydroxy, amino, C_{1-6} alkoxy, unsubstituted or substituted aryloxy, unsubstituted or substituted benzyloxy, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, halo, trifluoromethyl, trifluoromethoxy, nitro, C_{1-6} alkyl, carboxy, alkoxycarbonyl, carbamoyl, C_{1-6} alkylcarbamoyl, or R_1 and R_2 together represent methylenedioxy, $-(\text{CH}=\text{CH})_{2-3}$ -, carbonyldioxy or carbonyldiamino.

2. A process for the preparation of a compound of formula (I) as defined in claim 1, or a salt thereof or a solvate thereof, which process comprises the amidation of a suitable carboxylic acid with a suitable amine.

3. A process for the preparation of a compound of formula (I) as defined in claim 1, or a salt thereof or a solvate thereof, which process comprises the amidation of a compound of formula (II)



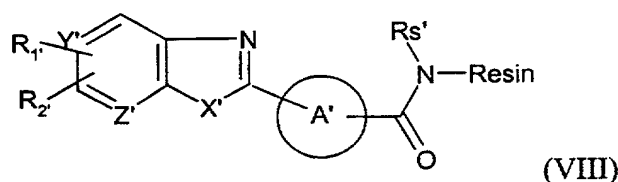
wherein X', Y', Z', A', R₁' and R₂' each respectively represent X, Y, Z, A, R₁ and R₂ respectively as defined in relation to formula (I) as defined in claim 1 or a protected form thereof with a compound of formula (III)



wherein R_S' and R_T' represent R_S and R_T respectively as defined in relation to formula (I) as defined in claim 1 or a protected form thereof and thereafter, as necessary, carrying out one or more of the following steps;

- 10 (i) converting one compound of formula (I) into another compound of formula (I);
 (ii) removing any protecting group;
 (iii) preparing a salt or a solvate of the compound so formed.

4. A process for the preparation of a compound of formula (I) as defined in claim 1,
 15 or a salt thereof or a solvate thereof, which process comprises the cleavage of a compound of formula (VIII) at the N-Resin bond.



- 20 wherein X', Y', Z', A', R₁', R₂', and R_S' each respectively represent X, Y, Z, A, R₁, R₂ and R_S respectively as defined in relation to formula (I) as defined in claim 1.

5. A pharmaceutical composition comprising a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, and a pharmaceutically acceptable carrier therefor.
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6. A method for the treatment and/or prophylaxis of diseases associated with over activity of osteoclasts in mammals which method comprises the administration of an effective non-toxic amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof.
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7. A method for the treatment of osteoporosis and related osteopenic diseases in a human or non-human mammal, which comprises administering an effective, non-toxic, amount of a compound of formula (I) according to claim 1 or a pharmaceutically
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acceptable salt thereof or a pharmaceutically acceptable solvate thereof, to a human or non-human mammal in need thereof.

8. A method for the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia, viral conditions (for example those involving Semliki Forest, Vesicular Stomatitis, Newcastle Disease, Influenza A and B, HIV viruses), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), autoimmune diseases and transplantation, for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS and Alzheimer's disease, angiogenic diseases, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours, in a human or non-human mammal, which method comprises administering an effective, non-toxic, amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, to a human or non-human mammal in need thereof.
9. A compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, for use as an active therapeutic substance.
10. A compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof and/or a pharmaceutically acceptable solvate thereof for use in the treatment and/or prophylaxis of diseases associated with over activity of osteoclasts in mammals.
11. A compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for use in the treatment of and/or prophylaxis of osteoporosis and related osteopenic diseases.
12. A compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof for use in the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia, viral conditions (for example those involving Semliki Forest, Vesicular Stomatitis, Newcastle Disease, Influenza A and B, HIV viruses), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), autoimmune diseases and transplantation, for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS and Alzheimer's disease, angiogenic diseases, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours, in a human or non-human mammal
13. Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, for the manufacture of a medicament for the treatment and/or prophylaxis of diseases associated with over activity of osteoclasts in mammals.

14. Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, for the manufacture of a medicament for the treatment and/or prophylaxis of osteoporosis and related osteopenic diseases.
15. Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof, for the manufacture of a medicament for the treatment of tumours, especially those related to renal cancer, melanoma, colon cancer, lung cancer and leukemia., viral conditions (for example those involving Semliki Forest, Vesicular Stomatitis, Newcastle Disease, Influenza A and B, HIV viruses), ulcers (for example chronic gastritis and peptic ulcer induced by *Helicobacter pylori*), autoimmune diseases and transplantation, for the treatment and/or prevention of hypercholesterolemic and atherosclerotic diseases, AIDS and Alzheimer's disease, angiogenic diseases, such as rheumatoid arthritis, diabetic retinopathy, psoriasis and solid tumours.

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

AZOLYLBENZAMIDES AND ANALOGUES AND THEIR USE FOR TREATING OSTEOPOROSIS

the specification of which (check one)

- ☐ is attached hereto.
☒ was filed on 23 June 2000 as Serial No. PCT/EP00/05881
and was amended on (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or Inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)

Number	Country	Filing Date	Priority Claimed
9914825.6	GREAT BRITAIN	24 June 1999	Yes

I hereby claim the benefit under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed below.

Application Number	Filing Date
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I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

Serial No.	Filing Date	Status
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I hereby appoint the practitioners associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and direct that all correspondence be addressed to that Customer Number:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

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